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Hyperactivity and reduced energy cost of physical activity in obese 5-HT2C mutant mice. L. ABDALLAH, K. NONOGAKI, L.H. TECOTT. *Dept. of Psychiatry, University of California San Francisco, San Francisco, CA 94143-0984, USA.*

We have shown that mice with a targeted null mutation of the 5-HT2C receptor gene display hyperphagia by 5 weeks of age and yet do not develop obesity until later in life (5-6 months). The development of obesity in these mice is not accompanied by increases in their degree of hyperphagia. Here we investigate the mechanisms by which young mutant mice compensate for their hyperphagia and how age-dependent failure of that compensation leads to weight gain. We report that young adult 5-HT2C receptor mutant mice have elevated home-cage activity levels, which can contribute to their ability to maintain normal body weight. However, similar to food intake, home cage hyperactivity is maintained in mutant mice at least up to 9 months of age and does not explain their late-onset obesity development. Also, no changes in resting metabolic rate were observed as indicated by normal resting energy expenditure as well as normal body temperature at both ages. However, simultaneous recording of oxygen consumption and locomotor activity in young (3 months) and older (9 months) mutant and wild type mice revealed that a decline in the energy cost of locomotor activity occurs with age, and that this decline is exacerbated in 5-HT2C receptor mutant mice. These data suggest that age-related decreases in the energy cost of physical activity might contribute to the development of middle-age obesity. Physiological mechanisms that underlie this process are under investigation.

Ethanol-conditioned flavor preferences in short daily sessions. K. ACKROFF, A. SCLAFANI. *Brooklyn College of CUNY, Brooklyn, NY 11210, USA.*

Ad lib-fed rats learned a strong preference (90%) for a saccharin-sweetened Kool-Aid flavor paired with concurrent volume-matched intragastric (IG) infusions of 5% ethanol over an IG water-paired flavor in 22 h/day sessions. Yet, initial attempts to obtain ethanol-conditioned flavor preferences using the same flavors and 30 min/day sessions were ineffective in ad lib and food-rationed rats. We next mimicked the parameters from a report of successful ethanol conditioning in deprived rats: a 0.5 g/kg dose of IG ethanol given 5 min before access to distinctive, intense HCl and NaCl flavors. Rats learned to prefer an ethanol-paired flavor when mixed in 5% sucrose but not in 0.2% saccharin. Then we tested the importance of the infusion-flavor delay using sucrose flavored with concentrated Kool-Aid (0.25%). Rats trained with 0.5 g/kg ethanol infused 5 min before or concurrent with intake of flavored sucrose learned a preference. This suggests that the 5-min delay is not critical but intense flavors in sucrose are required for ethanol-conditioned preference in short sessions. The reduced effectiveness of ethanol to condition preferences in short as opposed to long sessions contrasts with the robust conditioning actions of glucose but parallels results obtained with fructose. The preference reinforcing actions of ethanol, like those of fructose, may develop slowly and are thus most effective with long training sessions. Long sessions may also minimize potential aversive effects of ethanol. Supported by NIAAA grant AA11549.

Hormonal, metabolic and behavioral consequences of high intensity workloads in rats. T. ADAGE, B. ROORDA, G.H. VISSER, S. DAAN, A.J.W. SCHEURINK, *Dept. of Neuroendocrinology, University of Groningen, PO Box 14, 9750 AA Haren, The Netherlands.*

Hormonal, metabolic and behavioral consequences of (excessive) high intensity physical workloads were studied in rats. To this end, female Wistar rats were subjected to either a moderate or a maximal workload and the physiological differences between the groups were investigated during the course of the study (approx. 50 days, from voluntary running to maximal workload). Sedentary rats served as controls. Body weight, running activity and food intake were measured daily. Chronically implanted jugular catheters allowed stress-free blood sampling for measurement of resting levels of glucose, insulin, glucagon, catecholamines, ACTH and corticosterone along the study. An intravenous glucose tolerance test (IVGTT) was performed at maximal workload level to measure insulin sensitivity and glucose tolerance. Energy expenditure was assessed before the imposed workload schedule and at maximal intensity. Rats that ran at a (subjective) maximal workload reduced their body weight to

a new level (80% of the sedentary controls). Food intake, blood glucose levels, sympathetic outflow, HPA axis activity and circadian running patterns were significantly different between the groups. All runner groups showed reduced baseline insulin levels and (moderate) glucose intolerance in comparison to sedentary controls. The effects that were observed in the animals at their subjective maximal workload were remarkably similar to the pathophysiological changes that are reported in endurance athletes suffering from overtraining syndrome. We hypothesize that the subjective maximal workload may serve as an animal model for overtraining and possibly the burn out syndrome.

Moderate exercise stimulates GLP-1 release in healthy, normal-weight subjects. T.C.M. ADAM, M.S. WESTERTERP-PLANTENGA, *Nutrition Research Institute NUTRIM, Maastricht University, P.O. Box 616, 6200 MD Maastricht, The Netherlands.*

Glucagon-like peptide 1 (GLP-1), as an incretin, potentiates glucose-related insulin secretion at the level of pancreatic b-cells. Moreover, exercise has been shown to improve insulin sensitivity in humans with impaired glucose tolerance. It is not known whether exercise also affects GLP-1 release. To assess the effect of moderate exercise on GLP-1 (7-36 amide) secretion, we compared 10 healthy normal weight subjects performing exercise with 20 subjects who rested (14 men, 16 women; BMI 22.9±1.8; age 35.9±13yr; body fat% 22.9±8.3). Subjects arrived in a fasted state and performed the exercise test based on 25% of maximal power output/Wmax from an incremental exercise test for one hour or stayed in a resting supine position. Both groups stayed in a resting supined position the following hour and were requested to drink 250ml water. Blood samples were taken every 30min and GLP-1 was analyzed with an ELISA kit for non-radioactive quantification of biologically active forms of glucagon-like peptide. AUC of GLP-1 release was significantly increased during one hour of exercise compared to the resting condition ($p<.05$). We conclude that moderate short term exercise (1h) evoked elevated GLP-1 levels compared to a non-exercise control condition. This effect might support the beneficial effect of exercise on insulin sensitivity and metabolic fitness.

Blockade of central glucagon-like-peptide-1-receptors (GLP-1-R) prevents the short-term anorectic response to i.c.v. CART peptide (CARTp). S. AJA, C. EWING, T.H. MORAN, *Dept. Psychiatry, Johns Hopkins Univ. Sch. Med., Baltimore, MD 21205, USA.*

Central i.c.v. administration of CARTp reduces food intake, produces a conditioned taste aversion, reduces gastric emptying, and increases c-Fos production in brain areas involved in the control of feeding. Similar alterations are elicited by central administration of GLP-1. We explored the possibility that endogenous activation of central GLP-1-R is involved in the anorectic response to exogenous CARTp. Male Sprague-Dawley rats with lateral ventricular cannulas were trained to consume Ensure during scheduled 30-min access. Rats were given a GLP-1-R antagonist, des-His1, Glu9-exendin-4 (EX: 0, 10, 32, 100 µg), 10 min prior, and CART (55-102) (0, 1 µg) 5 min prior to Ensure access. CARTp given alone reduced intake of Ensure to 55% of control. CARTp reduced intake of Ensure similarly in the presence of 10 µg and 32 µg EX, but did not reduce food intake in presence of 100 µg EX. EX alone did not alter food intake at any dose. EX at 100 µg did not block the anorectic response to peripheral cholecystokinin (1 nmol/kg). Thus, prevention of an anorexia with EX was selective for that produced by CARTp. I.c.v. CARTp may reduce food intake through an endogenous GLP-1 release, and activation of central GLP-1-R.

Provoked hyperphagia in neonates and weight at weaning presage the mid-life obese phenotype of the 5-HT2C receptor KO mouse. S.F. AKANA, D. SAN JUAN, T. HOLSCHER, M. F. DALLMAN. *Dept. of Physiology, UCSF, San Francisco, CA 94143, USA*.

Serotonin is implicated in feeding disorders. We are studying the male mice from a genetic line lacking the serotonin 2C receptor (5-HT2CR; KO). The KO mice initially eat the same amount of food and maintain identical body weight to their wildtype (WT) controls in the first 6-12 weeks of life. Subsequently, KO mice develop hyperphagia leading to body weight (BW) gain and subsequent increase in fat mass. We routinely weighed our mice at weaning at 21 days and found that the male KOs were significantly heavier ($p=0.034$) than their WT siblings (KO=10.33 ± 0.22 grams; n=68, WT=9.69 ± 0.29 grams; n=44). Our breeding strategy is to mate heterozygous females with C57bl/J6 males, so it is unlikely that a difference in maternal behavior is altering the nutrition and care of the mice. A genotype difference at weaning could be due to differences in intake. To test this hypothesis we measured 2h food intake in 10d-old pups. We removed the dam from the nesting cage and the pups were kept warm. 2h later, the hungry pups were sexed, numbered, stroked with a paintbrush in the anogenital region to void the bladder and weighed. The pups were then placed in individual cups and allowed to suckle paper towels soaked in half-and-half cream for 30m. The pups were reweighed and

the increase in BW measured. KO pups ate significantly more (p=.0376; WT=0.178 mg, n=17, KO=0.250 mg, n=11). We conclude that the 5-HT2C receptor is involved in two types of hyperphagia. (supported by MH57967 and DK28172).

Effect of melatonin in female and male rats fed two-way choices of sensorily contrasting macronutrients. K. ANGERS, L. THIBAULT, *School of Dietetics and Human Nutrition, Macdonald Campus of McGill University, Montréal, Canada.*

The objective of the study was to examine the effects of melatonin, a hormone that triggers biological rhythms, on macronutrient selection. Forty-eight adult Wistar rats of both sexes were divided into 3 groups, with each group being offered a simultaneous ad libitum choice of two diets: a carbohydrate-rich diet and a protein-rich diet. The 3 groups differed in the type of carbohydrate and protein being offered, and macronutrient intakes following administration of various doses of melatonin (i.p.) at dark onset were examined. Melatonin increased casein diet intake (4 h following administration) in female rats at a dose of 10,000 pg/ml blood and in male rats at doses of 3,000 pg/ml and 10,000 pg/ml. Melatonin also increased soy isolate and egg protein diets intake in male rats at doses of 10,000 pg/ml and 6000 pg/ml, respectively. Over the 12 h that followed melatonin administration (10,000 pg/ml), male rats displayed augmented intake from dextrin/cornstarch, cornstarch and sucrose/cornstarch diets. We can conclude that melatonin has short-term effects on protein intake and long-term effects on carbohydrate intake. Acknowledgement: research supported by the Natural Sciences and Engineering Research Council of Canada (NSERC).

Influence of different anesthesia and blood sampling procedures on plasma levels of metabolites and corticosterone in rats. M. ARNOLD, W. LANGHANS**,** *Institute of Animal Sciences, Swiss Federal Institute of Technology (ETH), 8603 Schwerzenbach, Switzerland*.

Various blood sampling techniques are commonly applied in studies of ingestive behavior and metabolism in laboratory animals, and many of them require anesthesia, which itself may affect the parameter of interest. Those effects have rarely been characterized. We assessed the effects of 4 anesthesia procedures (ether [E] or isoflurane [I] inhalation, intraperitoneal injection of xylazin/ketamine [XK] or medetomidine/midazolam/fentanyl [MMF]) in combination with jugular vein blood sampling, and two anesthesia-free sampling procedures (puncture of the vena saphena [VS], tail incision [T]) on plasma concentrations of glucose, lactate, free fatty acids (FFA), and corticosterone. Compared to results of jugular vein blood samples from non-anesthetized, freely moving rats [NA] rats, plasma glucose was 14 [I] to 44 [MMF] % higher in all samples collected in anesthesia and 12-14% lower in VS and T samples, respectively. Plasma lactate was 26 [MMF] to 100 [E] % higher in all samples obtained in anesthesia and extremely high in VS and T samples (226 and 140% increase, respectively). Plasma FFA concentration was 10 [I] to 25 [MMF] % lower in samples obtained in anesthesia and 14-52 % higher in VS and T samples, respectively. Finally, plasma corticosterone was 250 [I] to 524 [E] % higher in samples obtained in anesthesia and 28 and 38 % higher in VS and T samples, respectively. Thus, various anesthesia and blood sampling procedures lead to dramatically different metabolic findings. This should be considered for the design and interpretation of blood sampling experiments in laboratory animals.

Amphetamine cross-sensitizes to sugar, producing increased locomotor activity and subsequent sugar consumption. N.M. AVENA, B.G. HOEBEL, *Dept. of Psychology, Princeton University, Princeton, NJ 08544, USA.*

The goal was to determine the locomotor and consummatory effects of sugar in amphetamine-sensitized rats. Following a 30-minute baseline locomotor activity measure, male rats were administered either 3.0 mg/kg amphetamine or saline i.p. daily for 6 days. On the final day of injections, locomotor activity was again measured for 30 minutes. Experiment 1: Seven days later, half of each group was allowed to drink 10% sucrose or water for 1 minute in their home cages, followed by a final 30-minute locomotor activity test to determine whether or not the animals had become hyperactive in response to sugar. Amphetamine-sensitized animals showed an increase in locomotor activity following a taste of sugar, but not water ($p<.03$) compared to saline-treated animals ($p<.05$). Experiment 2: All subjects were then given access to 10% sucrose for 1 hr daily for five consecutive days. Sucrose intake was recorded. The amphetamine-sensitized group had higher sucrose intake over the five day measurement period ($p<.01$). These results suggest that sugar may be acting on the same system as amphetamine to trigger hyperactivity, and that alterations in this system caused by repeated doses of amphetamine can cause an appetite for sugar that lasts at least a week. Supported by USPHS grant DA-10608 and Wyeth Research

What can we learn from animal models for Anorexia Nervosa? Y. AVRAHAM, S. HAU, O. BONNE, E-L, MARCUS, S. SHOHAM, E. M. BERRY, *Dept of Human Nutrition & Metabolism, and Psychiatry, Hebrew University-Hadassah Medical School, and Herzog Hospital, Jerusalem, Israel.*

Our research attempts to model some enigmas concerning the psychobiology of Anorexia nervosa (AN) to answer the following questions. 1). Could some of the cognitive and psychological disturbances be due to the lack of nutritional precursors for neurotransmitters, resulting from semi-starvation? 2). Why are there such different clinical responses to the stress of weight loss? 3). What "pleasure" do patients get instead of food? We have developed three models in mice - Diet restriction (DR), separation stress and activity ? to mimic some of the clinical features of AN. We found that mild caloric restriction (60% DR) increased learning ability whereas this was severely impaired after 40% DR. However, cognitive function was restored by tyrosine, the dietary precursor of catecholamine neurotransmitters. DR was also accompanied by alterations in the balance between the sympathetic and parasympathetic systems and in the expression of the M1 muscarinic receptor. Despite similar degrees of weight loss, the three models showed significantly different responses in central noradrenergic activity and the hypothalamic- pituitary-adrenal responses in ACTH and corticosterone production. In separate experiments in rats, using immunohistochemical techniques, we have found that there is an increase in enkephalin and dynorphin activity. And further, the effect in DR of anandamide, the endogenous agonist of the endocannabinoid system derived from dietary linoleate, is similar to many of the actions of tyrosine. It is hoped that these data will lead to a better understanding of the disease, and even suggest potential novel dietary therapeutic approaches.

Characterization of controls of feeding in db/db mice with transgenic neural specific replacement of the functional (LEPR-B) leptin receptor. A.V. AZZARA, S. CHUA, H. B. SCHIÖTH, G.J. SCHWARTZ, *Dept. Psychiatry, NY Hospital-Weill Cornell Medical College, White Plains, NY 10605, Uppsala University, Dept. of Neuroscience, Uppsala, Sweden, and Barrie Diabetes Research Center, Columbia University NY, NY 10013 USA.*

Mutant *db/db* mice are hyperphagic and obese due to a deficiency of the B isoform of the leptin receptor. Transgenic replacement of this LEPR isoform under the control of the neural specific enolase promoter (NSE-Rb) partially normalizes the obese phenotype. To assess the role of the central LEPR-B replacement in the control of ingestion, we evaluated food intake and meal parameters during spontaneous and scheduled liquid meals in female NSE-Rb mice and *db/db* background controls. NSE-Rb mice had reduced spontaneous food intake and meal size relative to *db/db* controls, and the decrease in meal size was characterized by a significant reduction in burst number. Lateral intracerebroventricular (icv) injections of leptin (6-10 ug /2 µl) reduced body weight and 22h food intake in NSE-Rb mice but not *db/db* controls. In NSE-Rb mice, Neuropeptide Y (NPY) (5 µg icv) increased 4 h daytime intake, with an increase in meal number. Central administration of the selective melanocortin 4 receptor antagonist HS014 also increased food intake and meal size. These data demonstrate: 1) that transgenic replacement of LEPR-B restores the feeding inhibitory effects of central exogenous leptin and normalizes some controls of meal size and food intake, and 2) that central NPY and melanocortin signalling pathways, putative downstream mediators of central leptin's actions, are functional in this model. Supported by DK47208 (GJS), DK26687 (SC), DK57621 (SC).

Anatomical substrates and CRH receptor subtype mediation of urocortin-induced anorexia. V.P. BAKSHI, S.M. NEWMAN, L.E. WEINBERG, N.H. KALIN, *Dept. of Psychiatry, University of Wisconsin at Madison, Madison, WI 53719, USA.*

Urocortin is an endogenous ligand for the two cloned receptors within the corticotropin-releasing hormone (CRH) system, which is the primary neuroendocrine regulator of stress responses. Immunohistochemical studies have revealed a dense urocortin-containing terminal field within the lateral septum (LS), a forebrain limbic structure that contains high levels of CRH2 receptors but is devoid of the CRH1 receptor subtype. Urocortin infusion into hypothalamic sites decreases feeding, however the effects on ingestive behavior of urocortin infusion into the LS are unknown. The present studies sought to determine if 1) urocortin infusion into LS disrupted ingestive behaviors 2) urocortin-induced effects were mediated selectively by the CRH2 receptor subtype. Separate groups of mildly food-restricted rats received infusions of urocortin (0, 50, 125, 250 ng/0.5 ml) into either the LS, the lateral ventricle (LV), or the medial caudate (MC). Urocortin decreased feeding and drinking while concomitantly increasing several displacement behaviors such as grooming and orofacial stereotypies after infusion into LS but not LV or MC. Separate animals received intra-LS infusions of either the CRH1-selective antagonist NBI27914 (0 or 1 µg/0.5 µl), the CRH2-selective antagonist Astressin2B (0, 500 ng, or 1 µg/0.5 µl), or the mixed CRH1/CRH2 antagonist d-Phe-CRH(12-41) (0, 100 ng, or 1 µg/0.5 µl) before

receiving intra-LS infusions of vehicle or urocortin (250 ng/0.5 µl). Pretreatment with the mixed CRH1/CRH2 antagonist or the selective CRH2 antagonist but not the CRH1 antagonist reduced urocortin-induced behaviors. These findings indicate that LS CRH2 receptors may play an important role in regulating ingestive behaviors.

Studies on nucleus accumbens-hypopthalamus interactions in the control of feeding behavior. B.A. BALDO, C.F. LANDRY, A.E. KELLEY, Dept. Psychiatry, *University of Wisconsin-Madison Medical School, Madison, WI 53719, USA.*

Blockade of glutamate receptors or stimulation of gamma amino butyric acid (GABA) receptors in the nucleus accumbens (Acb) shell produces intense hyperphagia thought to result from a functional interaction between the Acb shell and the lateral hypothalamus. Pharmacologically inactivating the lateral hypothalamus blocks hyperphagia elicited from the Acb shell, and feeding-related manipulations of the Acb shell increase expression of the immediate early gene product, Fos, in the lateral hypothalamus and other hypothalamic regions. We have conducted a number of studies extending these results. First, we explored whether infusions of muscimol, a GABA receptor agonist, into the Acb shell induces Fos expression in hypothalamic neurons containing either melanin concentrating hormone (MCH) or orexin/hypocretin. Intra-Acb shell muscimol produced a slight increase Fos expression in orexin/hypocretin-containing cells but not in cells containing MCH. Fos expression was also induced in a cluster of cells ventral to the fornix that contained neither orexin/hypocretin nor MCH. Interestingly, we noted a considerable number of orexin/hypocretin-containing fibers in the caudal Acb shell, although infusions of hypocretin/orexin into the Acb shell did not increase feeding behavior. Second, a microinfusion study was conducted to test whether insulin or leptin would block hyperphagia produced by intra-Acb shell muscimol infusions. Neither intraventricular insulin nor intraventricular leptin infusions significantly reduced intra-Acb shell muscimol-induced feeding. In summary, feeding elicited from the Acb shell activates anatomically selective hypothalamic cell populations, and these feeding responses may bypass to some degree adiposity-signaling factors, like insulin and leptin, that normally limit food intake.

Injection of threonine (THR) into the anterior piriform cortex (APC) alters meal patterns within the first 4 hours of exposure to a THR imbalanced diet (IMB). J.A. BARRETT, B.G. TRUONG, D.W. GIETZEN, *School of Veterinary Medicine, Dept. of Anatomy, Physiology and Cell Biology, Univ. Calif. Davis, Davis, CA 95616, USA*.

Animals fed a THR limiting diet (IMB) after a low protein diet, reduce their food intake to approximately 50% of control by 6h. Meal patterns have not been examined in detail for hrs 1-4 after diet introduction, corresponding to the time of the CS-US conditioning interval for amino acids described by Booth (1973). Here, 14 rats were implanted with bilateral cannulae into the APC. After recovery, they were prefed a basal diet on an 18hr feeding schedule. On the experimental day, the animals were injected with either 2nmol THR or saline into the APC, given IMB, and meal patterns were recorded for 6hr. Animals given THR injections consumed more IMB than saline injected animals (5.67 +/- 0.55g vs 4.03 +/- 0.37 g for 6hr, respectively, $p<0.05$), as expected. THR injected animals had longer first meals than controls $p<0.05$, but no differences in amount eaten in meal 1; all first meals were completed within hr 1. During the 1-4h period, THR injected animals spent more time eating (31.6 +/- 2.2min) than controls (14.9 +/- 4.8min, $p<0.005$) at similar rates. The increased food intake resulting from APC THR injections included a shorter intermeal interval between the 1st and 2nd meals (1.3 +/- 0.2 vs 2.7 +/- 0.6 hr) and a larger 2nd meal (1.6 +/- 0.3 vs 0.7 +/- 0.3, $p<0.05$). The 2nd meal onset was 1.5h after THR injection vs 3h after saline. Thus, THR injection delayed development of the expected aversion during the first 4h. Supported by NIH NS33347, USDA 2000-01049.

Peripheral mechanisms for detecting amino acids. G.K. BEAUCHAMP, A.A. BACHMANOV, *Monell Chemical Senses Center, 3500 Market Street, Philadelphia, PA 19104, USA.*

Free amino acids are present in many foods and they are often detectable by their taste. Amino acids have been described as having characteristic sweet, bitter, sour, salty and umami tastes. In addition, amino acids are often described as having taste qualities that do not fit into any of these standard categories. Recently, there has been substantial progress in identifying candidate receptors for umami-tasting amino acids and sweet amino acids. A large family of bitter taste receptors may be involved in detecting some bitter amino acids as well. Nevertheless, a full understanding of the peripheral mechanisms for detecting and recognizing amino acids remains elusive. Additional receptor mechanisms, as yet unidentified, are likely to exist and their identification will aid in understanding peripheral processes involved in regulation of amino acid and protein status.

The effects of intermittent nicotine (NIC) administration on meal patterns in female rats. L.L. BELLINGER, P.J. WELLMAN, *Dept. Biomed. Sci., Texas A&M Univ. Sys. HSC, Dallas, TX 75246 and Dept. Psychol. Texas A&M Univ., College Station, TX 77843, USA*.

NIC is known to decrease food intake (FI) and body weight (BW). Daily NIC usage in man is intermittent, yet many previous studies of NIC effects on FI and BW have given it continuously. In the present study female Sprague Dawley rats were housed in computerized FI modules and fed 45 mg rodent pellets. Starting on the day of estrous the rats were injected i.p. with saline or 4 mg/kg/day of NIC, in four equal amounts, during the dark phase for 13 days and the rats followed for 13 days, thereafter. FI was significantly reduced only during NIC injection. BW was significantly decreased starting on day 3 and until day 24, thus BW was reduced after cessation of NIC despite normalization of FI. These data were similar to our earlier findings in male rats (Soc. Neurosci. Vol. 27: Program No. 947.15, 2001). MPA revealed only a trend for increased meal number during NIC treatment, which contrasts our earlier finding of increased meal number in male rats. Similar to our male data meal size was reduced ($P<0.05$) during 13 days of NIC treatment, but in contrast to the male data not thereafter. Meal duration was ($P<0.05$) reduced only during the first week of NIC treatment. These data show that when NIC is given intermittently the female rat shows a prolonged decrease in body weight even after cessation of NIC. MPA showed the reduced FI during NIC administration is due to a decrease in meal size. Compared to our earlier male study there are distinct gender differences in meal pattern responses to NIC. Supported by TAMUS-HSC Tobacco Funds grant 2000-22.

Increased dietary fat attenuates the anorexic effects of intracerebroventricular MTII in rats. S.C. BENOIT, D.J. CLEGG, E.L. AIR, A. JACKMAN, P. TSO, D.A. D'ALESSIO, S.C. WOODS, R.J. SEELEY, *Depts of Psychiatry, Pathology and Medicine, University of Cincinnati, Cincinnati, OH 45267-0559, USA.*

Considerable evidence suggests that the hypothalamic melanocortin (MC) system plays an important role in the control of food intake and energy balance. An important unanswered question is whether diets high in fat attenuate melanocortin signaling, which may contribute to dietary-induced obesity. Therefore, we compared the efficacy of the MC receptor agonist, MTII, to reduce food intake in rats maintained on either a high-fat or low-fat diet, carefully matched for all other nutrient content. After 12 weeks of maintenance on these diets, rats were cannulated and MTII (0.0, 0.01, 0.1, 0.3, 1.0 nmoles) was administered i3vt. Results of the dose-response curves suggest that MTII was less effective to reduce food intake in rats maintained on the high fat diet. Using real-time PCR, we also assessed whole-hypothalamic expression of the MC agonist precursor gene, POMC, in rats maintained on each diet. Despite significantly higher plasma leptin and insulin levels, POMC gene expression was not greater in rats maintained on the high-fat diet. Moreover, the high-fat pair-fed rats (consuming the same number of calories as the low-fat-fed rats) had significantly lower POMC than both other groups. These results support the hypothesis that consumption of a high-fat diet alters the hypothalamic melanocortin system, which may contribute to dietary-induced obesity.

Interstitial glucose concentration in the hypothalamus of rats during hypoglycemia. J.L. BEVERLY, M.G. DE VRIES, N. GUEDET, L.M. ARSENEAU, *Dept. of Animal Sciences, University of Illinois, Urbana, IL 61801, USA*

The ventromedial hypothalamus (VMH) is involved in the feeding and compensatory responses to glucoprivation have been well documented. The firing rates of glucose responsive neurons in the VMH are altered by changes in interstitial glucose concentration and are affected by glucoprivation. Extracellular concentrations of glucose in the hypothalamus have not been reported. Using microdialysis probes (membranes: 0.2 x 1.0 mm) placed into the VMH, glucose concentrations of male Sprague-Dawley rats (250-300 g) were determined using an enzyme-linked fluorometric assay. Basal glucose concentrations of 1.50 ± 0.20 mM decreased to 0.84 ± 0.15 mM during the first 20-30 min after insulin administration (0.5 or 5.0 U insulin kg-1). After an initial lag, changes in VMH glucose closely paralleled changes in blood glucose; remaining at approximately 20% of blood glucose concentration during the 60 min following insulin treatment. Interstitial glucose concentrations in the VMH were also evaluated in overnight fasted rats using the No Net Flux method in a cross-over designed experiment. Glucose concentrations of1.40 ± 0.08 mM were decreased to 0.73 ± 0.05 mM ($p<0.001$) in rats in which food was withheld for approx. 16 hr. VMH glucose, as a percent of blood glucose concentration decreased from 18.7± 1.4% to 13.8 ± 0.8% ($p<0.01$). Ambient glucose levels in the VMH are reduced in parallel with blood glucose levels during insulin-induced hypoglycemia to a level shown in vitro to alter activity of certain neuronal populations in the VMH. Glucose concentrations in the VMH are reduced to a similar magnitude by an overnight fast.

Hypothalamic corticotropin-releasing factor gene overexpression may contribute to voluntary exercise-induced anorexia of rats. S. BI, E.E. LADENHEIM, T.H. MORAN, *Dept. of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.*

Access to a running wheel and the resulting activity produce alterations in food intake characterized by increased meal size, decreased meal frequency, overall anorexia and body weight loss. To understand the bases of these phenomena, we assessed circulating hormone levels and hypothalamic gene expression for neuropeptide Y (NPY), proopiomelanocortin (POMC), and corticotropin-releasing factor (CRF) in Sprague-Dawley rats with and without access to a running wheel. We found running wheel activity significantly decreased circulating leptin levels, whereas plasma corticosterone levels were significantly increased. Consistent with decreased leptin levels, arcuate nucleus (ARC) NPY gene expression was up-regulated and POMC gene expression was down-regulated. In contrast, CRF gene expression was up-regulated in both the paraventricular nucleus (PVN) and dorsal hypothalamic area (DH) in running wheel rats even though these rats had lower leptin and higher corticosterone levels. Furthermore, we found that NPY gene expression was increased in the dorsomedial hypothalamus (DMH) in response to intense exercise. We suggest that DMH NPY gene overexpression may contribute to the exercise-induced increase in meal size, and PVN and DH CRF gene overexpression may underlie the overall anorexia and body weight loss seen in rats with running wheel access. (Supported by DK19302 and DK57609).

The hypothalamic pituitary adrenal axis in female subjects suffering from bulimia nervosa. G.S. BIRKETVEDT, R. OLSTAD, J. SUNDSFJORD, J. FLORHOLMEN, *Laboratory of Gastroenterology, Institute of Clinical Medicine, University of Tromsø, Norway*

The eating disorder bulimia nervosa has been associated with impaired satiety, decreased resting metabolic rate and abnormal neuroendocrine regulation. The aim of this study was to investigate the diurnal cortisol secretion in subjects suffering from bulimia nervosa. Five female bulimic subjects, age 24-56, and 5 sex- and weight-matched controls participated in the study. The bulimic subjects were all in a stable phase of the disease with no purging or over-eating. The subjects recorded food intake and hunger sensation for 7 days. Then, after an overnight fast they were admitted to the Clinical Research Center for a 24 hour recording of cortisol. The blood samples were drawn every 2nd hour from 8 AM. All bulimics reported increased sensation of hunger during the day, with a maximum in the evening. In both groups the diurnal cortisol secretion showed a peak at 8 AM, with lowest secretion between 12 PM and 2 AM. The maximum and minimum levels did not differ between the two groups. In the bulimic group there was an additional secretional peak between 22 PM and 6 PM. There were no differences in the diurnal maximum and minimum levels of cortisol secretion between bulimic subject and control subjects. An additional peak of cortisol secretion was observed in the afternoon and early evening in the bulimics. This parallelled the time of increased hunger sensation during the day. This apparent dysregulation of diurnal cortisol secretion may contribute to the increased hunger sensation in bulimic subjects.

Hypertrophia of the adrenal gland in one subject suffering from the Night Eating Syndrome. G.S. BIRKETVEDT, D. AVENARIUS, J. STØRMER, J. SUNDSFJORD, J. FLORHOLMEN, *Laboratory of Gastroenterology, Institute of Clinical Medicine, University of Tromsø, Dept. of Radiology and Dept. of Clinical Chemistry, University Hospital of Tromsø, Tromsø, Norway.*

In 1999 we reported night eaters to suffer from neuroendocrine disorders, including diurnal hypersecretion of cortisol. Recently, we reported a blunted response to corticotropin releasing hormone (CRH) in night eaters. In this study we tested the hypothesis that night eaters have hypertrophia of the adrenal gland as a result of an over-expressed hypothalamic-pituitary-adrenal axis. One female night eater underwent computor tomography (CT) of the adrenal gland. Twelve night eaters and 12 controls had previously performed a 24 hrs blood sampling test. In 5 night eaters and 5 controls a 120 min CRH test (100 ug i.v.) had been performed. Cortisol and adrenocorticotropin hormone (ACTH) in blood were measured by radioimmuno assays. The female nighteater had an increased size of the adrenal gland (unilateral). She was otherwise healthy. In this night eater the 24 hrs plasma cortisol profile showed increased levels between 8 AM to 11 PM when compared to the controls. In the CRH test the maximal increase of ACTH from baseline value was 7 ng/ml in the night eater and 21.0 ± 10.8 ng/ml (mean ± SD) in the control subjects. The maximal increase in cortisol from the baseline values was 19 nmol/l in the night eater and 230 ± 73 nmol/l in the control subjects. We present a night eater with increased diurnal cortisol secretion, a blunted response of ACTH and cortisol in response to CRH, and a hypertrophia of the adrenal gland. This association may be causal.

Comparison of a very low-carbohydrate diet and a calorie-restricted low-fat diet on reported calorie intake and body weight. B. BREHM, S.R. DANIELS, D.A. D'ALESSIO*, University of Cincinnati, OH 267-0559, USA.*

The role of specific macronutrients in the control of food intake and body weight remains controversial. While standard medical advice typically involves eating diets relatively low in fat and saturated fat, several popular weight loss regimens advocate high fat, high protein and very low carbohydrate. We sought to compare the effect of these different macronutrient diets on weight loss, reported caloric intake and cardiovascular risk factors. We randomly assigned 53 healthy, obese women (mean BMI of 33.6 + 0.3 kg/m2) to six months of either a very low-carbohydrate diet or a calorie-restricted diet with 30% of calories as fat, conforming to currently accepted dietary guidelines. Weight, body composition, blood pressure, and circulating concentrations of lipids, glucose, insulin, leptin, and b-hydroxybutyrate were assessed before and after three, and six months on the diet. Baseline intake in both groups was similar and women on both diets reduced calorie consumption by comparable amounts when assessed at three and six months. Women on the very low-carbohydrate diet lost more weight (8.5 + 1.0 vs. 3.9 + 1.0 kg; $p<0.01$) and more body fat (4.8 + 0.67 vs. 2.0 + 0.75 kg; $p<0.01$) than those on the low-fat diet. Mean levels of blood pressure and fasting glucose were within normal ranges in both groups. Our results indicate that a very low-carbohydrate diet is more effective than a low-fat diet for weight and body fat loss and is not associated with measurable deleterious effects on cardiovascular risk factors in healthy women over a six-month period.

Development of pathways from the arcuate nucleus implicated in neural control of feeding behavior in mice. S. BOURET, *ORPRC and Oregon Health Science University, Division of Neuroscience, Beaverton, OR 97006, USA.*

The arcuate nucleus of the hypothalamus (ARH) is a critical component of forebrain pathways that regulate a variety of neuroendocrine functions and plays a particularly important role in relaying leptin signals to other parts of the hypothalamus. Consistent with this functional role, we have demonstrated that the ARH sends strong projections to the paraventricular nucleus (PVH), the dorsomedial nucleus (DMH), and the lateral hypothalamic area (LHA), all of which have been implicated in the regulation of feeding and metabolism. Intriguingly, neonatal rodents do not respond to leptin treatment in the same way as do adults suggesting that certain aspects of the leptin signaling pathways in the hypothalamus may not be mature. Therefore, we examined the ontogeny of projections from the ARH. Our studies revealed that the major ARH projection pathways develop within distinct temporal domains during the first two weeks of life, with the innervation of the DMH occurring first, followed by PVH innervation, and then by LHA innervation. In addition, preliminary findings suggest that absence of the postnatal leptin surge leads to an abnormal development of projections from the ARH. Taken together, these findings provide insight into the development of central control of food intake and body weight as well as the role of leptin in neonatal animals. Supported by NIH Grants DK55819, NS37952 and RR00163.

The hypocretins in the nucleus accumbens: linking sleep with reward mechanisms B. BOUTREL, V. FABRE, G. MARTIN, G.F. KOOB, L. DE LECEA, *Depts. of Neuropharmacology and Molecular Biology, The Scripps Research Institute, La Jolla, CA 92037, USA.*

The hypocretins (hcrt1 and hcrt2), also known as orexins, are two neuropeptides derived from the same precursor, expressed in a few thousand cells in the lateral hypothalamus. Hypocretin-containing cells project throughout the brain, including ascending projections to the olfactory bulb and cerebral cortex, through the medial septum and the nucleus accumbens. Here we have studied the interactions of the hypocretins with different neurotransmitters by patch clamp recording of acutely dissociated cells from the nucleus accumbens. Application of hcrt1 or hcrt2 decreased postsynaptic NMDA currents, enhanced GABA currents but did not affect glycine-activated conductances. Our results strongly suggest that in contrast to other brain regions, the hypocretin peptides may be inhibitory in the NAcc, probably via binding hcrt receptor 2. To determine whether the hypocretins have a functional role in the modulation of circuits governing excessive drug intake and reward mechanisms, we have determined the concentration of hcrt1 peptide in the hypothalamus and NAcc of rats that had been submitted to a short and long term access administration paradigm of cocaine. Preliminary data indicate that hypocretin release is substantially increased during long-term but not short term access to drug. Withdrawal from a binge dose of cocaine causes a significant decrease in the levels of hypothalamic hcrts as determined by radioimmunoassay. Our results suggest that the hypocretinergic system integrates information and acts through multiple circuits to produce a coherent physiological output that results in the modulation of the states of arousal.

The effects of adrenalectomy and genetic background on carcass composition and neuropeptide Y5 receptor expression in lean and obese corpulent rats. L.M. BROWN, S. THOMAS, S.O. LIEU, C.T. HANSEN, T.W. CASTONGUAY, *Dept. of Nutrition and Food Science, University of Maryland, College Park, MD 20742, USA.*

Neuropeptide Y (NPY) is an important neuromodulator whose effects on feeding are most likely mediated by the Y1 and Y5 receptors. This experiment examines the effects of adrenal hormones on carcass composition and expression of the Y5 receptor in corpulent rats. Lean and obese male rats from three strains, LAN, SHR and DSS, were adrenalectomized (ADX) or sham operated. Food intake, corrected for spillage, and body weight were recorded daily. Plasma insulin, corticosterone and leptin were measured by RIA. NPY Y5 in situ hybridization was performed using an S35 labeled oligonucleotide unique to the Y5 receptor. All hypothalamic nuclei visible at bregma -3.30 mm were selected by densitometry. In addition, carcass composition was measured. ADX and sham obese LAN rats had higher percent of carcass fat than their respective lean controls. ADX only reduced percent of carcass fat in the obese group. ADX and sham obese LAN groups had lower percent of carcass protein than lean groups. ADX only increased percent of carcass protein in the obese group. Obese SHR and DSS rats had a higher percent of carcass fat and a lower percent of protein their lean controls. ADX did not significantly change carcass fat or protein. Contrary to expectation, NPY Y5 expression in the hypothalamus did not differ by strain, phenotype or surgical group. Summation of the hypothalamic nuclei may have masked any differences. It is also possible that another receptor (like Y1) is more closely linked to the plasma values in this model.

Preference learning in restrained and unrestrained eaters. J.M. BRUNSTROM[1], G.L. WITCOMB[1] S. HIGGS[2]. [1]*Human Sciences, Loughborough University, Loughborough, Leicestershire, LE11 3TU, UK.* [2]*School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK.*

Recently, Brunstrom et al., (2001, Appetite, 37, 197-206) found that female restrained eaters may be insensitive to flavor-preference learning. In their paradigm, participants were trained with instances of three novel flavors. Each was paired differentially with a candy reinforcer: 90%, 50%, or 10% of the time. After training, flavor-preference ratings from the unrestrained eaters were highly correlated with the reinforcement ratio. In contrast, restrained eaters exhibited no evidence for evaluative learning. In the present study, we sought to determine whether this failure represents a specific insensitivity to flavor-preference learning. This possibility was addressed by using abstract patterns as conditioned stimuli rather than flavors. Following Johnsrude et al., (1999, Learning & Motivation, 30, 250-264), three patterns were differentially paired with a candy reinforcer (90%, 50%, or 10%). In our version, chocolate was used as the unconditioned stimulus, and baseline measures of pattern preference were taken. Our results indicate that restrained eaters are also insensitive to this type of associative learning. In contrast, unrestrained eaters appear to learn - their change in preference for the patterns increased as a function of reinforcement ratio. This suggests that the failure of restrained eaters to show evaluative conditioning is not due to a specific inability to learn flavor preferences. Rather, it may be more general in nature. Given this possibility, we propose that further investigation of the relationship between associative learning and dietary restraint is now warranted.

Effects of estradiol on interleukin-1 beta-induced c-fos expression in female rats. P.C. BUTERA, J.J. TRIPLET, *Dept. of Psychology, Niagara University, NY 14109, USA*

Contact with infectious agents causes the release of proinflammatory cytokines, and interleukin-1 (IL-1) has been shown to elicit a collection of behavioral and physiological responses collectively known as "sickness behavior." Previous research indicates the effects of IL-1 on fever, activity, and food intake are modulated by ovarian hormones, although the neural mechanism for these estrogen/IL-1 interactions is unknown. We examined c-Fos-like immunoreactivity (Fos-like IR) in the paraventricular nucleus of the hypothalamus (PVN) and nucleus of the solitary tract (NTS) after IL-1 beta treatment in estradiol (EB) and oil-treated ovariectomized rats. These brain regions are important for the regulation of feeding behavior and show Fos-like IR after peripheral treatment with IL-1. In this experiment, animals were given SC injections of EB (20 ug) or the oil vehicle for 2 consecutive days. On the third day, rats received an IP injection of IL-1b (5 ug/kg) or .9% saline. Ninety minutes later, rats were perfused and brains were processed for Fos-like IR in the PVN and NTS. Estradiol pretreatment reduced the number of cells showing Fos-like IR in both the PVN and NTS. The results are consistent with the hypothesis that estradiol enhances the anorectic action of IL-1 by affecting the central processing of cytokine-induced signals in the NTS and/or the PVN.

The power of food scale: rationale and psychometric evaluation. M.L. BUTRYN, R. ANNUNZIATO, C. CRERAND, L. DIDIE, C. OCHNER, M.R. LOWE, *MCP Hahnemann University, Philadelphia, PA 19102-1192, USA.*

There are several measures of dietary control (restraint) and dietary abandon (overeating), but there is no measure of the psychological influence of the mere presence or availability of food. The 10-item Power of Food Scale (PFS) was developed to assess this construct. The PFS is a reliable measure (Cronbach's alpha = .93; test-retest reliability = .84). The construct validity of the PFS was examined by comparing it with Herman and Polivy's Restraint Scale (RS) in two studies. The hypothesis that the "power of food" may underlie effects associated with the RS was tested by comparing obese clinic attenders and restrained and unrestrained normal weight individuals on the PFS. Obese individuals and restrained eaters scored higher than unrestrained eaters (PFS means = 23.8, 25.2, and 17.4, respectively). In a second study with normal weight females, the PFS (which contains no items measuring overeating) was more strongly related to Disinhibition than the RS (ts = 6.98 versus 3.49) in a regression analysis. When the two items on the RS that explicitly measure overeating were removed from the RS total score, the correlation between the RS and disinhibition decreased from .57 ($p < .001$) to .19 ($p = .12$) and the amount of variance the 8-item RS explained in Disinhibition (with PFS scores held constant) decreased ($t = 2.09$, $p = .04$). These findings are consistent with the hypothesis that the PFS taps a dimension that explains why some people need to restrain their eating, particularly in an environment that promotes weight gain.

Sensitization of sugar-induced feeding: enhancement of the appetizer effect. C.A. CARRILLO, B.G. HOEBEL, *Dept. of Psychology, Princeton University, Princeton, NJ 08544, USA.*

In humans, the "appetizer effect" is an increase in food consumption caused by the ingestion of a premeal item such as a palatable food or alcohol. The present study investigates sensitization of the appetizer effect in rats as a function of previous dietary experience. Thirty male Sprague-Dawley rats were initially given a sugar appetizer (10 ml of 10% sugar for 10 min), and chow intake was measured for an hour. Animals (N=10/group) were then maintained for a week on one of three feeding conditions: (1) cycled chow—deprivation for 12 hr alternated with 12-hr access to chow, (2) cycled sugar and chow—deprivation for 12 hr alternated with 12-hr access to chow and 10% sugar, (3) cycled chow and ad lib sugar—ad lib access to 10% sugar and deprivation for 12 hr alternated with 12-hr access to chow. Animals were returned to ad lib chow and water for seven days, then a second appetizer test was administered. Only the group of animals cycled on sugar and chow displayed a significant increase in food consumption during the hour after presentation of the second appetizer ($p<0.01$). The results demonstrate that a short-term diet consisting of intermittent sugar and chow can cause a lasting change that such that a sugar appetizer is sensitized, leading to a greater intake of chow. Supported by grant DA-10608, Wyeth Research, and GEM Fellowship (to C.A.C.)

Starvation in anorexia nervosa: does the negative energy balance mobilize a biologically based survival mechanism? R.C. CASPER, *Stanford University School of Medicine, Stanford, CA 94305, USA.*

From a biological perspective, anorexia nervosa (AN) represents a condition of slow semistarvation as a result of voluntary food restriction. The severity of the catabolic changes depends on the size and duration of the caloric deficit and the nature of the nutritional deficit. For the most part, the physical and psychological symptoms in AN are noticeably alike those observed in voluntary or enforced starvation, notably those documented in the Minnesota experiments on human starvation. However, some psychobiological signs in AN, specifically a "paradoxical liveliness" and a "remarkable and strikingly disproportionate abundance of physical energy" have not been described in other starvation states. Energy expenditure studies have shown normal or increased physical activity levels in underweight and untreated AN patients. We have suggested that in individuals vulnerable to AN a phylogenetically programmed link between lack of food and motility which functions in rodents becomes operative. This hypothesis offers an explanation for the denial of illness and lack of concern in AN, in fact a high initiative and normal energy levels would be expected to support resistance to weight gain. Neurotransmitters, hormones and peptides which might be involved in the motility inducing effects in rodents and in sustaining mental and physical arousal in AN will be discussed.

Delayed gastrointestinal transit in patients with hepatocellular carcinoma. C.-Y. CHEN, F.-Y. CHANG, S.-D. LEE, *Division of Gastroenterology, Department of Medicine, Taipei Taiwan 10642, Taiwan.*

Disturbed gastrointestinal (GI) motility exists in cirrhotic patients; however, less is known about the character of GI transit in hepatocellular carcinoma (HCC) patients. It is interesting to study the GI transit in HCC patients and to explore the patient factors modulating GI transit. A non-invasive hydrogen breath test which measured the orocecal transit time (OCTT) was used to study GI transit in 40 HCC patients, 20 cirrhotics and 40 age- and sex-matched healthy volunteers with normal bowel habits. Meanwhile, their clinical manifestations and various blood parameters, such as platelet count, prothrombin time, erythrocyte sedimentation rate, etc. were collected. The plasma endothelin-1 and nitrate/nitrite levels were also measured. The OCTTs were delayed in HCC and cirrhotic patients compared to controls (116.3 ± 7.8 and 104.5 ± 10.6 vs 75.3 ± 5.1 min, $P < 0.05$). Neither the severity of liver damage, presence of ascites, tumor size, portal hypertension, nor various blood parameters, such as nitrate/nitrite, endothelin-1, platelet count, etc, had any influence on GI transit. Only serum alpha-fetoprotein levels exhibited a trend toward positive correlation with the OCTTs ($r = 0.271$, $P = 0.091$). HCC patients have delayed GI transit. The confounding factor responsible to disturb GI transit in HCC patients needs further exploration.

Effect of NMDA antagonism on lithium-induced conditioned taste aversion in male rats. S.H. CHOI[1], T.A. HOUPT[1], B.S. KWON[2], D.G. KIM[1], J.W. JAHNG[1], *[1]Dept. of Pharmacology, Yonsei University College of Medicine, Seodaemoon-gu Seoul outside of U.S 120-752, South Korea, [2]Dept. Biological Science, The Florida State University, Tallahassee, FL 32306, USA.*

Lithium chloride is a widely used unconditioned stimulus in conditioned taste aversion (CTA) learning. Intraperitoneal injection of lithium chloride at large dose induces transient expression of c-Fos in the hypothalamic paraventricular nucleus (PVN), central nucleus of amygdala (CeA), and nucleus tractus of solitarius (NTS), and c-Fos induction in these brain regions is known to have a correlation with CTA formation. It has been reported that NMDA receptor antagonisms affect CTA learning and NMDA receptors are richly localized in the hypothalamus and brainstem, areas implicated in CTA learning. We examined lithium-induced CTA in male rats with central or peripheral administration of MK-801, a non-competitive NMDA receptor antagonist, 30 min prior to the lithium injection at the conditioning, and the brain Fos expression was also examined by c-Fos immunohistochemistry. Neither systemic (100ug/kg, ip), nor central (5ug/5ul, icv) MK-801 produced modulatory effects on the CTA induced by isotonic lithium chloride (12ml/kg, ip). Lithium-induced c-Fos expression was significantly attenuated in the PVN (22% decrease), NTS (43%), but not in the CeA by systemic MK-801. Mild, but a significant CTA produced by systemic, but not by central, MK-801, although systemic MK-801 did not significantly induce c-Fos expression in all three brain regions examined, that is, PVN, CeA, NTS. We conclude that lithium-induced CTA formation may not be mediated by NMDA receptor, although lithium-induced neuronal activation significantly decreased by MK-801 pretreatment in the hypothalamus and brainstem, and peripheral effect of NMDA antagonism might have contributed to the formation of aversive memory by MK-801.

Are overweight adults able to predict the preprandial glycemia by subjective feelings after training as accurately as lean adults do? M. CIAMPOLINI, M. VAN WEEREN, B. DE PONT, W. DE HAAN, L BORSELLI, *Dept. of Pediatrics, University of Florence, Italy.*

Objective. Training adults to recognize glycemia at emergence of mild depletion feelings. Design: Within individual verification of the apprehended ability. Subjects: 65 healthy adults, 27 males and 38 females (18 to 60 years) investigated for functional complaint (41 NW) or overweight (24 OW).Intervention: Subjects matched meal intake to the presumed inter-meal expenditure, and consumed copious amounts of fruit-vegetables to provoke the emergence of mild depletion feelings before mealtimes. They trained themselves by measuring glycemia at the perception of the same depletion feeling, generally gastric. Subjects started meals within one hour from recognition of this glycemia level. Two months later, subjects came to the Unit, and declared whether or not they perceived depletion and the presumed glycemia, which was then measured by the hexokinase method in the hospital laboratory. Results: 25 subjects perceived depletion and measured glycemia at 3.98±0.53(SD)mmol/l. 40 subjects did not perceive depletion and measured glycemia at 4.93±0.47mmol/l (P=10-9). The absolute approximation in the presumption was 6.8±6.0% of the measured value. The agreement limits (mean±2SD) were -19% and +17.6% of the mean measurement. The genders had no difference in the approximation (M:6.8±6.1% vs. F:6.6±5.7%). The OW and NW subjects also showed no difference in the mean approximation, which respectively was 5.6±3.7% and 7.3±6.6% of the measurement. Conclusion: Mild depletion feelings emerged as reliable threshold under 5mmol/l in 25/65 trained adults. 5/65 further subjects failed any threshold recognition under 4.5mmol/l, but presumed the glycemia with 4.2±2.7% approximation. 1/65 failed threshold and low glycemia recognition, presumably for no morning training.

Inhibition of CRF-induced anorexia by orphanin FQ/nociceptin: search for the site of action. R. CICCOCIOPPO, A. FEDELI, M. MASSI, *Dept. of Pharmacological Sciences and Experimental Medicine, University of Camerino, 62032 CAMERINO, Italy.*

Orphanin FQ/nociceptin (OFQ/N) inhibits CRF-induced anorexia in rats. The present study evaluated the sensitivity of forebrain sites to the effect of OFQ/N on CRF-induced anorexia in male Wistar rats. Animals were food deprived for 20 h, injected into the lateral cerebroventricle (LV) with 200 ng/rat of CRF or its vehicle, and given access to food 20 min after CRF injection. OFQ/N, 50, 100 or 1000 ng/rat, was microinjected into the bed nucleus of the stria terminalis (BNST), the paraventricular nucleus (PVN), the ventromedial hypothalamus (VHM), the central nucleus of the amygdala (CeA), the dorsal raphe nucleus (DR), or the LV, 10 min before CRF injection. In the BNST OFQ/N significantly reduced CRF-induced anorexia even at 50 ng/rat, while it was ineffective following injection in the PVN, VMH, CeA or DR at doses up to 1000 ng/rat. In the LV a significant effect was detected at 1000 ng/rat. Injected into the BNST OFQ/N, 50-1000 ng/rat, modified neither food intake in food deprived rats (not injected with CRF), nor feeding in freely feeding rats. CRF did not evoke anorexia following injection into the BNST. The present results confirm that OFQ/N antagonizes the anorectic effect of CRF in rats at doses that are not hyperphagic per se. Moreover, the BNST is highly sensitive to this effect of OFQ/N. The observation that CRF did not induce anorexia following injection in the BNST suggests that the effects of the two peptides are evoked at different sites and supports the idea of functional antagonism between them.

Comparison of central and peripheral administration of C75 on food intake, body weight, and conditioned taste aversion. D.J. CLEGG, M.D. WORTMAN, S.C. BENOIT, C.C. MCOSKER, R.J. SEELEY, *Dept. of Psychiatry, University of Cincinnati, Cincinnati, OH 45267-0559, USA*.

Fatty Acid Synthase (FAS) catalyzes the reductive synthesis of long-chain fatty acids from acetyl-coenzyme A (acetyl-CoA) and malonyl-CoA. C75 is an inhibitor of FAS, and potently reduces food intake and causes profound loss of body weight in mice. FAS is an ubiquitous enzyme that has been described primarily in liver, fat and muscle. We compared the relative behavioral responses to C75 when administered either centrally (third ventricle, i3vt) or peripherally (IP). While the threshold dose for IP C75 to reduce food intake was 10 mg/kg, the threshold dose for reducing food intake i3vt was 3 µg. Such data argue for FAS activity in the CNS as a potent target for the actions of C75. We also measured the ability of doses of C75 that produce reductions in food intake either centrally or peripherally to reduce consumption of NaCl after whole-body sodium depletion or produce conditioned taste aversions. Our results suggest that the anorexia produced by IP C75 is accompanied by visceral illness, whereas the anorexia produced by i3vt is not. Finally, we compared the effectiveness of C75 to reduce food intake on a diet that is more like the western diet (40% fat by kcals) than standard rodent chow (4% fat by kcals). C75 was equally effective in reducing food intake on both diets. Thus, the efficacy of C75 is not influenced by relative rates of glucose and lipid oxidation making FAS inhibition a potentially viable strategy for obesity therapy.

A Comparison of the role of leptin and insulin action in the CNS to regulate energy and reproduction in male and female rats. D.J. CLEGG, C.A. RIEDY, K.A. BLAKE SMITH, S.C. BENOIT, S.C. WOODS, *Dept. of Psychiatry, University of Cincinnati, Cincinnati, OH 45267-0559, USA.*

The distribution of fat in the body differs between males and females and is also associated with the relative secretion of the two “adiposity” hormones, leptin and insulin. We report that the brains of male and female rats are differentially sensitive to these two hormones in terms of the effect on food intake, body weight, and age at puberty. Leptin (3.5 µg/2 µl) or saline (2 µl) were administered into the third ventricle of age and weight matched males and females. Leptin significantly reduced intake in females ($P < 0.05$) but had no effect in males. The same rats were administered insulin (4 mU/2 µl) or saline (2 µl), and the males were significantly ($P < 0.05$) more sensitive to insulin than were females. The melanocortin system has a pivotal role in controlling food intake and is a downstream target for both leptin and insulin’s catabolic actions in the brain. We found that there were no gender differences in sensitivity to a variety of doses (.01, 0.1, 0.3, 1.0 nmol/2 µl) of MTII, a non-specific melanocortin receptor agonist. These results suggest that the gender differences in sensitivity to leptin and insulin occur upstream of the melanocortin receptors. Additionally, intraventricular leptin but not insulin lowered the age at which vaginal opening occurred. Because insulin and leptin reflect different fat beds and are differentially distributed in males and females, the implication is that males and females regulate adiposity-relevant parameters differently.

Attenuation of CCK satiation by NMDA ion channel blockade depends on post-oral feedback but not on increased gastric emptying. M. COVASA[1], R C. RITTER[2], G.A. BURNS[2], [1]Dept. of Nutrition, *The Pennsylvania State University, University Park, PA 16802 and [2]Dept. of VCAPP, Washington State University, Pullman, WA 99164-6520, USA.*

Previously we and others demonstrated that MK-801, a non-competitive NMDA antagonist, increases meal size and delays satiation following injection of CCK. We also demonstrated that MK-801 increases gastric emptying of a liquid meal. CCK inhibits gastric emptying, and it is possible that MK-801 attenuates CCK-induced satiation by reversing inhibition of gastric emptying. Since CCK-induced inhibition on sham feeding does not depend on inhibition of gastric emptying we examined the ability of MK-801 to reverse CCK-induced satiation in sham feeding rats. MK-801 (100 µg/kg, IP) alone did not alter 30-min sham intake of 15% sucrose, compared with intake after saline. CCK-8 (2 or 4 µg/kg, IP) reduced sham intake. MK-801 did not attenuate reduction of sham feeding by CCK. This result suggests that MK-801 does not directly antagonize CCK-satiation signals, and is compatible with the hypothesis that MK-801 attenuates CCK inhibition of gastric emptying. However, our measures of MK-801's ability to reverse CCK-induced inhibition of gastric emptying did not support this hypothesis. MK-801 (100 µg/kg, IP) accelerated 10 min emptying (3.9 + 0.2 mls) compared to control (2.72 + 0.2 mls). CCK-8 (0.5 µg/kg, IP) reduced gastric emptying to1.36 + 0.3 mls. However, pretreatment with MK-801 did not attenuate CCK-8-induced reduction of emptying (0.9 + 0.4 mls). We conclude that MK-801-induced attenuation of CCK-satiation during real feeding, as well as MK-801-induced increases in meal size, must involve interference with other post-oral signals derived from mechanical or chemical properties of the meal. Supported by NIDDK-52849 and NS-20561.

Hindbrain Fos expression and intestinal satiation depend on carbohydrate hydrolysis not glucose absorption. M. COVASA[1], R.C. RITTER[2]. [1]Dept. of Nutrition, *The Pennsylvania State University, University Park, PA 16802 and [2]Dept. of VCAPP, Washington State University, Pullman, WA 99164-6520, USA.*

Intestinal infusion of carbohydrate produces satiation and postabsorbtive hyperglycemia. We previously demonstrated that satiation by maltotriose, a product of starch digestion, depends on its hydrolysis to glucose, but does not require glucose absorption. Inhibition of food intake by intestinal carbohydrates is mediated by capsaicin-sensitive vagal sensory neurons, and is accompanied by increased nuclear Fos expression in the dorsal vagal complex. To determine whether activation of vagal sensory pathways by intestinal carbohydrate requires hydrolysis to glucose or glucose absorption, we examined Fos expression in the dorsal vagal complex, following intraintestinal co-infusion of glucose or maltotriose along with an inhibitor of either amyloglucosidases (acarbose, 0.2%, w/v) or an antagonist of the glucose transporter, SGLT-1 (phlorizin, 0.39%, w/v). Intestinal infusion of maltotriose (180mM) or glucose (694mM) produced a significant increase in nuclear Fos immunoreactivity in the dorsal vagal complex. Co-infusion of acarbose attenuated maltotriose-induced, but not glucose-induced Fos expression in the dorsal vagal complex. Co-infusion of phlorizin along with maltotriose or glucose did not reduce increased Fos immunoreactivity induced by either carbohydrate. These results indicate that vagal activation by glucose oligosaccharides requires hydrolysis to glucose, but not glucose absorption. Together with previous findings, these data suggest that satiation and vagal activation by glucose carbohydrates is mediated by an interaction of glucose with a glucoreceptor on the luminal side of the intestinal epithelium. Supported by NS-20561.

Suppression of food intake by intragastric ethyl oleate in normal and vagotomized rats. J.E. COX, A. RANDICH, S.T. MELLER, G.R. KELM, *Dept. of Psychology, University of Alabama at Birmingham, Birmingham, AL 35294, and Health Science Institute, Procter and Gamble, Mason, OH, USA.*

We have previously reported that repeated jejunal infusions of long-chain fatty acids suppress caloric intake, weight gain, and body fat. Here we report two experiments revealing similar effects of intragastric infusions of ethyl oleate (EO). In the first experiment, two groups of adult, male Sprague-Dawley rats with chronic gastric catheters received bolus infusions of either 5 ml of a 34% emulsion of EO (load = 1.7 g; 15 kcal) or vehicle (N=10 in each group). Infusions were delivered on 10 consecutive days 30-45 min prior to onset of the dark phase, at which time rats were given access to liquid diet (vanilla-flavored Boost, Mead-Johnson). Compared to controls, the group receiving EO decreased its voluntary intake by an average of 24.2 kcal/day, significantly in excess of calories infused ($P<.05$). Weight gain was reduced by 41% ($P<.01$). In the second experiment, rats with subdiaphragmatic vagotomy (N=11) or sham vagotomy (N=8) received intragastric infusions of vehicle on two consecutive days followed by two days of treatment with 34% EO. Vagotomy attenuated EO-induced suppression of cumulative food intake by approximately 50% at 3, 6, and 23 h (P's < .005).Thus, like intrajejunal

linoleic acid, intragastric EO reduces total caloric intake and does so via mechanisms both dependent upon and independent of the vagus. (Supported by The Procter and Gamble Company)

Effects of central administration of ethanol on behavior and cFos IR. D.L. CRANKSHAW, J.E. BRIGGS, C.J. BILLINGTON, A.S. LEVINE, *Minnesota Obeisty Center, VA Medical Center, Minneapolis, MN 55417, USA.*

The initial role of the central nervous system in the acquisition of alcohol addiction is poorly understood. We evaluated whether centrally administered ETOH would induce a conditioned taste preference (CTP) or aversion (CTA) and alter cFos immunoreactivity (cFos-IR) levels in brain regions associated with feeding, aversion, and/or reward. Acute ETOH{ICV} as tested in the alcohol naïve rat did not induce CTA nor effect the amount of water imbibed by treated rats. The effects of ETOH{ICV} on intake and preference were determined using two novel solutions: a palatable (i.e. sweet) noncaloric 0.1% saccharin or a noncaloric, unsweetened KoolAid-flavored water. A single dose of ETOH{ICV} in the ethanol-naïve animal induced a CTP for flavored water and a conditioned taste preference acceptance (CTPA) for saccharin, indicating that caloric value and palatability factors are not required for induction of preference. ETOH{ICV} significantly increased cFos-IR in a limited number of brain sites associated with feeding and reward including the bed nucleus of the stria terminalis, lateral dorsal area (BSTLD) ($p=.0034$), nucleus accumbens, shell area (Acb-sh) ($p=.0156$), paraventricular nucleus (PVN) ($p<.0001$), and lateral septum, ventral area (LSV) ($p=.0362$). Additionally, naloxone (3mg/kg bwt. sc), a general opioid antagonist blocked ETOH{ICV}-induced intake of saccharin, ($p=.0001$). Also, ETOH{ICV}-induced flavor preference was blocked for a limited amount of time with peripheral naloxone, ($p=.0005$). Further, there was a rebound in ETOH{ICV}-induced preference from the naloxone suppression. These data suggest that ethanol activates brain reward circuitry indicating a direct neural mechanism for the reinforcing nature of ethanol.

Paraventricular nucleus administration of DOI potentiates the inhibitory effect of urocortin on neuropeptide Y stimulated eating and respiratory quotient. P.J. CURRIE, C.D. COIRO, R. DUENAS, *Dept. of Psychology, Barnard College, Columbia University, New York, NY 10027, USA.*

Neuropeptide Y (NPY) is a 36 amino acid peptide hormone distributed throughout the mammalian CNS. The peptide plays an integral role in the control of ingestive behavior and energy metabolism. Microinjection of NPY into the hypothalamic paraventricular nucleus (PVN) stimulates eating, alters body temperature, and potentiates carbohydrate oxidation. In contrast, we have recently shown that PVN injection of urocortin, a corticotropin releasing hormone-related ligand, inhibits food intake, suppresses respiratory quotient (RQ) and antagonizes the action of NPY on feeding and RQ. Similarly, PVN injection of the 5-HT2A/2C receptor agonist DOI also attenuates NPY's effects. In the current study, we investigated the effect of DOI-UCN coinjection on the feeding and metabolic (RQ) action of NPY. In rats with unilateral PVN cannula, DOI (5-10 nmol) and UCN (12.5-25 pmol) were administered 10 min prior to the start of the dark cycle. NPY (100 pmol) was infused at dark onset. NPY alone stimulated eating and in a separate group of rats, elevated RQ, measured using an open-circuit calorimeter. PVN coinjection of DOI and UCN effectively reversed both effects suggesting that 5-HT and UCN act within the PVN to modulate the feeding and metabolic action of NPY.

Dorsal and median raphe nuclei injections of 8-OH-DPAT differentially inhibit the anorectic action of fluoxetine in female and male rats. P.J. CURRIE, M. BRAVER, M. KHAN, K. SRICHAROON, *Dept. of Psychology, Barnard College, Columbia University, New York, NY 10027, USA.*

Administration of the selective serotonin reuptake inhibitor fluoxetine (FLU) suppresses food intake under free-feeding and food-restricted conditions in both male and female rats. In the present study, rats were pretreated with the 5-HT1A agonist, 8-OH-DPAT, in an attempt to reverse FLU's inhibitory effect on feeding. 8-0H-DPAT was injected into either the dorsal or median raphe of male ($n=16$) and female ($n=16$) rats at doses of 0.1-0.4 nmol. FLU was injected IP at a dose of 2 mg/kg. Both compounds were administered just prior to the onset of the dark cycle. Dorsal and median raphe injections of 8-OH-DPAT dose-dependently reversed FLU's anorectic effect in male rats. In female rats, however, 8-OH-DPAT was largely ineffective in suppressing the feeding inhibitory action of FLU. These findings suggest that male and female rats are differentially sensitive to the ability of 5-HT1A receptor agonists to antagonize the feeding suppressive effects of FLU.

Sucrose makes the (stressed) body better. M.F. DALLMAN, A. BHARGAVA, L.R. SORIANO, K. LAUGERO, S.F. AKANA, M.E. BELL, *Dept. of Physiology, UCSF, San Francisco, CA 94143, USA.*

Both sucrose to drink (S) and corticosterone (B) restore body weight (BW) gain, UCP-1, fat depot mass, food intake, and central corticotropin-releasing factor mRNA to normal in adrenalectomized (ADX) rats. Carbohydrate ingestion increased pain thresholds, modifies behaviors and ↓ stress responses in people and rats. Here, we tested the interactions between sucrose and circulating B on behavioral, metabolic, autonomic and neuroendocrine responses to the stress of cold. Rats were left intact, sham-ADX, or ADX and replaced with pellets that provided normal (30%B) or high (100%B) constant circulating concentrations of B ± sucrose. More sucrose was drunk in the cold than at room temperature (RT), provided that [B] were > mean daily basal values in cold. Similarly, when [B] were elevated, rats not allowed S ate more chow in the cold than at RT. Neither increased sucrose nor increased chow ingestion occurred in cold if the rats were ADX 30%B. Although 30%B did not restore sucrose or feeding to normal, sucrose-drinking in this group ameliorated responses to cold. BW gain, fat depots weights, plasma insulin and testosterone as well as Tc were not different from sham-ADX rats in cold. By contrast, 30%B rats not drinking sucrose fared poorly, and none of the metabolic or endocrine variables were similar to shams. Responses of the ADX100%B group to cold resembled those of intact rats not drinking sucrose; however, these rats were metabolically abnormal at RT. We conclude that drinking sucrose ↓ stress-induced B while ↓ many responses to cold; elevated B is essential for the normal integrated cold-responses to occur. (supported by DK28172, T32DK07418, and a NARSAD Young Investigator Award.)

Phosphorylation of mitogen-activated protein kinase (MAPK) in the rat hypothalamus by a melanocortin receptor agonist. D. DANIELS[1], S.J. FLUHARTY[2], *Depts. of Animal Biology[1,2], Pharmacology[2], Psychology[2] and the Institute of Neurological Sciences[2], University of Pennsylvania, Philadelphia, PA 19104, USA.*

There is increasing evidence that melanocortins mediate at least some of the downstream effects of leptin action in the CNS through melanocortin-containing projections from the hypothalamic arcuate nucleus to the paraventricular nucleus of the hypothalamus (PVN). Although the complexity and long duration of the behavioral effects of melanocortins on food intake are strongly suggestive of underlying changes in gene expression, the mechanism by which these changes may occur remains to be determined. The present experiments used immunohistochemistry to demonstrate melanocortin-induced phosphorylation (activation) of MAPK in the PVN after lateral ventricular injections of the melanocortin agonist MTII into male rats. The number of phosphorylated MAPK-immunoreactive neurons was greater in animals injected with MTII (1 nmol; n=5) compared to controls (saline-injected, n=5; non-injected, n=3). Analysis of the rostral-caudal distribution of the labeled neurons revealed a main effect of treatment group ($p= 0.00178$), but neither a main effect of rostral-caudal distribution nor an interaction was detected. Although future experiments are necessary to determine the effect of concomitant administration of agonist and antagonist, these data are the first to suggest a coupling of central melanocortin receptors with this signal transduction cascade and may describe a mechanism through which the behavioral actions of melanocortins are mediated. Supported by NIH grants MH43787 and DK50218.

NPY and AgRP increases food hoarding more than food intake in Siberian hamsters. D.E. DAY, T.J. BARTNESS, *Dept. of Biology & Center for Behavioral Neuroscience, Georgia State University, Atlanta, GA 30303, USA.*

Neuropeptide Y (NPY) and agouti-related protein (AgRP) are colocalized in arcuate neurons and both appear to be involved in stimulating food intake (FI) because: 1) conditions that elicit increases in FI increase NPY and AgRP gene expression/protein content and 2) either peptide administered intracerebroventricularly (icv) markedly stimulate FI. Some data suggest that NPY draws animals to food rather than strictly increasing FI. Therefore, we tested whether NPY, two NPY receptor subtype agonists implicated in FI stimulation (NPY1 and NPY5 agonists) as well as AgRP altered foraging, food hoarding and FI by Siberian hamsters. Hamsters were housed in a simulated burrow system where completion of 10 or 50 wheel revolutions triggered food pellet delivery. Third ventricular injections of NPY or a NPY Y5 agonist at the start of the dark period significantly increased FI, but not foraging (pellets earned), especially 1-4h post injection. Icv injections of a NPY Y1 agonist or AgRP significantly increased food hoarding, but had little or no effect on FI. Thus, NPY, NPY1 receptor subtype stimulation and AgRP increased food hoarding more than FI, but did not stimulate foraging. In addition, it appears that the NPY Y5 receptor is more involved in feeding, whereas the NPY Y1 receptor is more involved in food hoarding. Finally, this semi-natural model appears ideal to investigate the effects of neuropeptides on appetitive versus consummatory ingestive behaviors.

A General Model of Intake Regulation. J.M. DE CASTRO, S. PLUNKETT, *Dept. of Psychology, Georgia State University, Atlanta, GA 30303, USA.*

Previously proposed models of intake regulation focus on specific variables thought to influence overall intake, and include factors involved in a reciprocal negative feedback on intake. These models, however, cannot account for the observations of prolonged and increasing deviations from defended levels, weakness and transitoriness of compensatory responses, the presence of powerful factors that are not compensated, and behavioral genetic data suggesting that there are a wide variety of independent genetic influences on numerous factors that influence intake. We propose a new general model of intake regulation in which intake is influenced by both a set of uncompensated factors that are not influenced by intake and by a set of compensated factors that are. The preferred levels of intake and both sets of factors are specified as influenced by heredity. Further, the model includes impact factors, weights, which specify the magnitude of the effect each factor on intake. The weights are assumed to be different for different individuals and their values are determined by heredity. A computer simulation of the new model demonstrated that it maintains different levels depending upon the external and internal environments, that changes in these environments result in new levels, and that inherited individual differences in responsiveness to these factors can markedly influence the levels obtained. The proposed general model appears to fit existing knowledge and is parsimonious and widely applicable.

Increased energy expenditure and uncoupling protein 2 and 3 expression, with normal locomotor activity and in vitro leptin production in obesity-resistant complement 3/acylation stimulating protein knockout mice. E.K. DIGITALE, O. NICOLESCU, K.L. STANHOPE, K. CIANFLONE, P.J. HAVEL, *Dept. of Nutrition, University of California, Davis, CA 95616, USA,* and *McGill University, Montreal, Canada.*

Mice deficient in complement factor 3 (C3), and consequently unable to produce acylation stimulating protein (ASP), are lean and obesity-resistant, despite increased food intake (~20%), and have low circulating leptin levels compared to wild-type (WT) animals (Endocrinology 2000). To further phenotype energy metabolism and endocrine function, we compared 24 h energy expenditure (EE) and physical activity, expression of uncoupling proteins (UCP) 1, 2, and 3, and leptin production in isolated adipocytes from C3/ASP knockout (KO) and WT mice. Twenty-four h EE was increased by ~12% in KO (587±16 vs 522±8 kcal/kg/24 h; $p<0.01$), but locomotor activity (12.0±2.9 vs 10.3 ±2.4 m/24 h) was not different between KO and WT. UCP-1 expression in brown adipose tissue was not increased in KO mice. In contrast, UCP-2 expression tended to be increased in adipose tissue, and UCP-3 in skeletal muscle was increased by 295% ($p<0.01$) in KO. Basal leptin production from cultured adipocytes was not different and insulin (1.6 nM) stimulated leptin production to a similar extent (+ 33.0±7.2 vs +36.0±11.8 ng/96 h) in KO and WT. In summary, 24 hour EE, but not physical activity, is increased and leptin production is unchanged in C3/ASP KO mice. Elevated EE cannot be explained by increased UCP-1 expression, however UCP-2 and 3 expression are increased. Low leptin levels in KO mice are not due to reduced leptin production, but probably reflect decreased adiposity and/or increased leptin sensitivity. Increased EE is likely to contribute to the lean, obesity-resistant phenotype in C3/ASP KO mice, despite significant hyperphagia.

Fenfluramine-induced hypophagia is increased during estrus in female rats. D.P. DIXON, H.M. RIVERA, L.A. ECKEL, *Program in Neuroscience, Florida State University, Tallahassee, Florida 32306, USA.*

Drugs that enhance serotonergic neurotransmission, including fenfluramine, potently inhibit feeding in rats. Some studies suggest this action of fenfluramine is greater in female than in male rats. Here, we examined whether fenfluramine-induced hypophagia varies across the estrous cycle. Female rats ($n = 8$) were housed in cages connected to running wheels (RWs). During baseline, food intake and RW activity were examined across one estrous cycle. Next, a within-subjects, counter-balanced design was used to examine the effects of fenfluramine on food intake and RW activity during diestrus, when food intake is maximal, and during estrus, when food intake is minimal. On test days, rats were i.p. injected with fenfluramine (1.0 mg/kg) or vehicle 30 min prior to dark onset. Fenfluramine-induced reductions in food intake were significantly greater during estrus than during diestrus at 2, 6, 12, and 24 h following drug treatment (e.g., reduction in food intake at 2h: diestrus, 48% vs. estrus, 83%, $P < 0.001$). Fenfluramine treatment also reduced RW activity by ~ 65 %, but this effect did not differ between diestrous and estrous phases. Food intake and RW activity on days in which rats did not receive injections were comparable to baseline values. These data demonstrate that sensitivity to the hypophagic effects of fenfluramine is increased during estrus. Additional studies are required to determine whether increased serotonin activity contributes to the decrease in food intake associated with estrus. Supported by NIH Joint Neuroscience Predoctoral Training Grant (NIH, NIDCR, NIGMS, NIMH, NINDS, NINR) and MH 63787.

Fenfluramine enhances activity-based anorexia in female rats. D.P. DIXON, L.A. ECKEL, *Program in Neuroscience, Florida State University, Tallahassee, Florida 32306, USA.*

Recent reports of elevated serotonin activity in women following recovery from anorexia nervosa suggest that serotonin is involved in the etiology or high relapse rates of anorexia nervosa. Here, we examined the effects of a serotonin agonist, fenfluramine, on the development of activity-based anorexia, an animal model of anorexia nervosa that promotes hypophagia, body weight loss, hyperactivity, and a disruption of the estrous cycle in food-restricted rats given free access to running wheels. Female rats (n = 16) were maintained on a restricted-feeding schedule in which food was available for 2 h per day, beginning 1 h after dark onset. Each day, 1.5 h prior to food access, rats received a single i.p. injection of 0.50 mg/kg fenfluramine or vehicle. When individual rats lost 25% of their baseline body weight (range = 5 - 8 d) daily drug treatment was terminated and food was freely available until baseline body weight was regained. Fenfluramine significantly reduced average daily food intake by ~ 30 % and decreased the latency to reach the 25% body weight loss criterion by ~ 2 d. During food restriction, running wheel activity and estrous cycle disruptions were similar between groups. The return to baseline body weight (range = 4 - 14 d) was not affected by prior fenfluramine treatment. These data suggest that increasing serotonin concentration concurrently with food restriction increases body weight loss associated with activity-based anorexia. Supported by NIH Joint Neuroscience Predoctoral Training Grant (NIH, NIDCR, NIGMS, NIMH, NINDS, NINR).

Expression of Fos protein following administration of mercaptoacetate in rat pups. A. DOERFLINGER, S.E. SWITHERS, *Dept. of Psychology, Purdue University, West Lafayette, IN 47907, USA.*

Administration of Mercaptoacetate (MA) elicits eating behavior in adult rats by stimulating vagal afferents, and produces increased neural activation in the brain as indexed by expression of the Fos protein product. MA has also been demonstrated to produce increased ingestive responding in rat pups aged 12 to 15 days. However, behavioral responses in pups are less robust than those seen in adults. Additionally, the behavioral alterations following administration of MA are accompanied by physiological changes representative of decreases in fatty acid oxidation. In the present study, Fos immunohistochemistry was used in 12-day-old rat pups to examine activation in neural pathways previously shown to express Fos following administration of MA in adult rats. Pups received an i.p. injection of 0 or 22.8 mg/kg MA, and were sacrificed 1 h later. Brains were processed, and Fos expression was examined in the DMX, NTS, AP, lPBN, CeA, and PVN. The results demonstrated that the pattern of c-fos activation in 12-day-old pups was significantly different from that seen in adult rats, consistent with the less robust behavioral activation produced by MA in pups compared to adults. In the CeA, there were significantly more cells expressing Fos-like immunohistochemistry following MA treatment; however, there were no significant differences between conditions in any of the other regions examined. Supported by NIDDK R01 55531 to SES.

Adrenalectomy increases sensitivity to central leptin- and melanocortin-induced anorexia. D.L. DRAZEN, D.J. CLEGG, M.W. SCHWARTZ, G. VAN DIJK, S.C. WOODS, R.J. SEELEY, *Dept. of Psychiatry, University of Cincinnati, Cincinnati, OH 45267, USA.*

Removal of adrenal steroids by adrenalectomy (ADX) reduces food intake and body weight in rodents and glucocorticoid replacement reverses these effects. This study examined the influence of the interaction between glucocorticoids and the leptin-melanocortin system on food intake and body weight. Glucocorticoids appear to influence food intake and body weight at least in part by decreasing leptin sensitivity, but the possibility that glucocorticoids influence activity downstream of leptin, such as the melanocortin system, is untested. We investigated whether the presence of glucocorticoids in normal rats reduces the sensitivity of the CNS to the food intake-reducing effects of melanocortins as well as leptin. Feeding responses were measured in 2 groups of rats: those in which circulating glucocorticoids were removed via ADX, and sham-operated controls. ADX rats were more sensitive to the anorexic actions of intracerebroventricular (icv) leptin than controls. Similarly, icv MTII, an MC3/4 receptor agonist, caused greater suppression of food intake in ADX (0.3 nM, 90%) compared to control animals (0.3 nM, 52%). The role of glucocorticoid deficiency in these effects of ADX was investigated by giving corticosterone in their drinking water, which restored sensitivity to both leptin and MTII to control levels. No differences between groups were found in hypothalamic leptin receptor mRNA expression. These results extend previous evidence that glucocorticoids promote food intake by reducing leptin sensitivity and we report similar effects on sensitivity to the anorexic actions of melanocortins. Increased senstivity to signaling via the leptin-melanocortin system may contribute to the weight-reducing effects of ADX.

Taste, cost, and energy density of foods. A. DREWNOWSKI, *Nutritional Sciences Program, School of Public Health and Community Medicine, University of Washington, Seattle, WA 98195, USA.*

Consumer food choices are determined primarily by considerations of taste, cost, and convenience and to a lesser extent by health and variety. Energy density of foods, their palatability, and their cost are all closely linked. Foods are palatable because they are energy dense; as a rule, energy-dense foods (e.g. chocolate) are preferred over energy-dilute foods (celery). The sheer availability of concentrated dietary energy is reinforcing to the hungry organism. The most palatable and most energy-dense foods in our food supply involve some combination of added sugar and fat. Added sugars and vegetable oils are among the cheapest sources of energy available, with sugar and fat accounting for 50% of energy in the American diet. Survey studies suggest that energy-dense foods are typically cheaper in terms of kcal/dollar that perishable foods with low energy density such as fresh produce. Growing portion sizes of energy-dense foods can be explained by their low cost. Economic analyses further show that cost constraints steer food choices toward higher-energy density diets. Generally, reducing energy density through increased consumption of vegetables and fruit cannot be accomplished without increasing food costs. Current studies suggest that not all diets cost the same; higher quality diets may be associated with higher costs. Structural and policy approaches to dietary change may be a promising complementary approach to current strategies for behavior change, most of which are aimed at individuals.

Increasing the portion size of a unit food increases energy intake. J.A. ELLO-MARTIN, L.S. ROE, J.S. MEENGS, D.E. WALL, B.J. ROLLS, *Nutrition Dept., The Pennsylvania State University, University Park, PA 16802, USA.*

Recent diet survey data indicate that Americans are consuming more energy than they have in the past. This increase has in part been attributed to the availability of larger portion sizes; however, there is limited research that has systematically examined the influence of portion size on energy intake. In the present study we incrementally increased the size of a food that was served as a single unit or piece, and examined the effect on intake at a single meal. Thirty-eight men and thirty-seven women ate lunch in the laboratory one day a week for four weeks. At each meal, subjects were served one of four submarine-type sandwiches that varied in portion size: 6, 8, 10, and 12 inches. The sandwich was consumed ad libitum. The order of presentation of the different sandwich sizes was randomized across subjects. Results showed that portion size significantly influenced intake at lunch for both men and women ($p < 0.0001$). When served the 12-inch compared to the 8-inch sandwich, men consumed 20% more energy (185 kcal) and women consumed 11% more energy (74 kcal). Despite significant increases in intake when served the 12-inch versus the 8-inch sandwich, ratings of hunger and fullness after the meal were not significantly different. These findings suggest that increases in the portion size of a unit food influence energy intake at a single meal, without differentially influencing subjective feelings of satiety. Thus, when consuming a unit food, energy intake depends on the size of the portion served. (Supported by DK59853).

Cortisol reactivity is related to taste perception among pre-menopausal women. E. EPEL, L. BARTOSHUK, *UCSF Psychiatry Dept., San Francisco, CA 94143, Dept. of Surgery, Yale University School of Medicine, New Haven, CT06520-8041, USA.*

Introduction: Stress and ingestive behavior are intricately linked, and the HPA axis plays an important mediating role in metabolism and possibly in taste perception. Previous studies have found that psychological distress is related to a genetic marker, PROP. We examined associations between stress-induced cortisol reactivity with taste perception of bitterness (PROP)in the laboratory. Method: We exposed healthy premenopausal women to a repeated laboratory stressor paradigm, to see whether this increased ratings of bitterness of PROP. Further, we assessed whether PROP perception was related to stress-induced cortisol secretion and psychological or anthropomorphic factors. Results: Exposure to stress dramatically increased the perceived intensity of PROP. High cortisol reactivity was related to increases in PROP sensitivity after stress, but also to lower PROP at each timepoint. PROP ratings after stress were marginally related to greater depression and chronic stress. Discussion: We will discuss several pathways through which stress and the HPA axis may influence taste perception. Future research should examine how stress and psychological factors may impact taste perception, which has implications for food choices, weight management, and disease risk.

Can chronic stress shape your body? Associations between stress-induced cortisol and abdominal fat distribution among lean and overweight premenopausal women. E. EPEL, B. MCEWEN, T. SEEMAN, K. MATTHEWS, J. ICKOVICS, *Dept. of Psychiatry, University of California, San Francisco, CA 94143, USA.*

The relationship between stress and weight gain may be different in rodents and humans. For example, rat studies often find that stress causes anorexia and weight loss, whereas human studies have mixed findings, including both weight loss and weight gain. Eating behavior may determine the differential weight changes, but across species, abdominal fat should be affected similarly by stress hormones. Specifically, stress may cause intra-abdominal fat mass to increase, regardless of changes in total body weight. Further, the clearest demonstration of the effect of stress on abdominal fat may be observed in lean people, because their abdominal fat may be due to stress hormones rather than to overall obesity. To study the relation between intra-abdominal fat and stress exposure, without the confound of obesity, we exposed both lean and overweight women with abdominal fat distribution (AFD) vs. peripheral fat distributions (PFD) to laboratory stress for three consecutive days. While all women with AFD reported greater chronic life stress and had higher adrenocortical responses to novel stress, the lean women with AFD showed the greatest vulnerability to stress. They displayed a significant lack of cortisol habituation to repeated stress and psychological traits indicative of defeat. These results suggest that chronic stress and cortisol reactivity may contribute to abdominal fat, and that the relation between chronic stress on body shape may be most apparent in lean women.

Inbred mouse strain differences in licking behavior to water and sucrose under water-restricted and non-restricted conditions. S. EYLAM, A.C. SPECTOR, *Dept. of Psychology, University of Florida, P.O. Box 112250, Gainesville, FL 32611, USA.*

We examined the phenotypic patterns of drinking behavior elicited by water and sucrose (0.05, 0.1, 0.2M) under two hydrational states in 3 inbred mouse strains previously shown to differ in their sweetener preference (C57BL/6J [B6], SWR/J [SWR], 129P3/J [129]). Mice (10/strain) were trained and tested daily in a computer-controlled apparatus in which free access to either stimulus was presented for 30 min in either a 23.5h water-deprived or nondeprived state. Although all mice were treated similarly there were striking differences in their licking patterns. SWR mice had a remarkably shorter mean interlick interval (92.6 ms) relative to the other two strains (B6=115.0 ms; 129=110.9 ms). All mice increased their total licking (and intake) as a function of both concentration and deprivation state, but did so in a strain-dependent way. When water deprived, 129 mice took significantly fewer and larger bursts and terminated their ingestion significantly earlier in the session compared with B6 mice. The pattern of SWR mice resembled that for 129 mice except that they tended to continue drinking longer into the session. The B6 mice licked 0.05M sucrose significantly more than the other strains especially when nondeprived, but this strain difference became much less notable as the concentration increased. We are currently in the process of extending our stimulus array and completing a more comprehensive analysis of the licking profiles of these mouse strains. Identification of these ingestive behavior strain differences may be useful in efforts to understand the neurobiological mechanisms subserving intake regulation. Supported by NIDCD R01-DC04574.

Developing a Scale to Measure Just About Anything: Comparisons Across Groups and Individuals. K. FAST, B. GREEN, L.M. BARTOSHUK, *Dept. of Otolaryngology, Yale University School of Medicine, New Haven, CT 06520-8041, USA*

It is a truth universally acknowledged, that a single man in possession of good fortune still cannot know the sensations of others. Most scales in sensory studies have limitations often overlooked: their labels do not denote the same absolute intensities to all. Labels like “very strong taste,” for example, denote more intense sensations to supertasters than nontasters of PROP (6-n-propylthiouracil). We have sought a remedy by using anchors (sensations, remembered sensations, labels) unrelated to taste. This lets us assume these anchors denote the same average intensity to each group. We add stability to such comparisons by adding more anchors. If we add enough, will we eventually be able to make valid comparisons across individuals? In the present study, subjects scaled sensations and intensity descriptors using magnitude estimation. When we expressed taste intensities relative to an anchor believed independent of taste (e.g., brightness of the sun), remembered taste sensations varied with bitterness of PROP; other remembered sensations (e.g., pressure, warmth, cold) did not. Normalized so that “strongest imaginable sensation of any kind” equals 100, supertasters rated the bitterness of black coffee 31.4, between a severe headache (27.8) and a broken bone (37.5) or scalding water (38.2). Nontasters rated the bitterness of black coffee 10.4, between the brightness of the moon (7.7) and the brightness of a fluorescent light (12.1). If enough anchors prove comparably positioned across individuals, this approach may not only allow across-group comparisons but across-individual comparisons as well.

Effects of brainstem ghrelin administration on meal patterning. L.F.H. FAULCONBRIDGE, J.M. KAPLAN, D.E. CUMMINGS[1], H.J. GRILL, *University of Pennsylvania, Dept. of Psychology,*

Philadelphia, PA 19104, USA, [1]University of Washington, VA Puget Sound Health Care System, Seattle, Washington, USA.

Ghrelin, an orexigenic peptide produced primarily in the stomach, is an endogenous ligand for the growth hormone secretagogue receptor (GHS-R). When administered centrally or peripherally, it increases food intake and body weight, and decreases fat utilization. In the present study, we explored the relevance of brainstem GHS-Rs and characterized the effect of ghrelin administration on meal patterning. In the first study, two ghrelin doses (1500pmol and 150pmol) were administered to the 3rd or 4th ventricles in the first hour of the light phase. Both doses caused significant increases in cumulative food intake over the subsequent three hours and there was no difference in effect between ventricles. In a separate experiment, we administered 1500pmol to the 4th ventricle and recorded food intake continuously over 24 hours. Ghrelin significantly decreased the latency to the first meal, resulting in an extra meal taken in the light phase. There is thus far little to suggest a reliable action of ghrelin on meal size or the behavioral structure of individual meals. We also found that administration of high-dose ghrelin in the early dark phase, when the probability of feeding is already high, had no effect on any parameter evaluated. The results affirm for the first time a brainstem (in addition to the recognized hypothalamic) site of action for the orexigenic effects of ghrelin. The meal patterning analyses are consistent with a principal appetitive role for ghrelin as a meal-initiating signal. DK21397 and DK42284.

Could hypothalamic catecholamines participate in the chronic control of protein ingestion? J.D. FERNSTROM, *Dept. of Psychiatry & UPMC Weight Management Center, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213, USA.*

To maintain nitrogen balance, mammals must chronically ingest an amount of protein that matches body protein losses. This protein requirement is typically modest in comparison to caloric intake. In their normal environments, animals ingest protein in modest excess of requirement. If protein intake exceeds requirement levels by much, amino acid catabolic enzymes are induced. It thus seems metabolically sensible that animals might regulate protein intake between requirement levels and that dietary level at which amino acid catabolic enzymes are induced. In rats, hypothalamic catecholamine synthesis varies directly with chronic protein intakes between 0% and 10% (% energy); the catecholamine changes are produced by a parallel variation in the brain concentration of tyrosine, the catecholamine precursor. The rat's maintenance protein requirement is 5-7%, and catabolic enzyme induction occurs at 10% protein intake. These catecholamine variations thus bracket the range of protein intakes most relevant to dietary protein adequacy, and thus could constitute a signal that the brain uses to insure adequacy of protein intake. Curiously, when given the choice, laboratory rats choose about 35% protein, 5-7-fold their requirement. This intake level makes little metabolic sense, and is much higher than that chosen by rats in the wild. Why lab rats elaborate this behavior is a metabolic mystery, and complicates the study of protein intake regulation.

Structural and policy approaches to dietary change. S.B. FOERSTER, *Dept. of Health Services, State of California, Sacramento, CA 95814, USA.*

Food choices and eating habits are strongly influenced by the environment, economics and society. The socially advantaged may have more options regarding diet and physical activity than do ethnic minorities and the poor. Strategies and programs for nutrition intervention increasingly rely on structural and policy approaches to dietary change as opposed to behavior change at the individual level. The State of California has implemented a number of programs to improve diets and health status at community level. Some of these programs are driven by legislation; others are developed in consultation with state and local health Dept.s, target communities and other key stakeholders. Among these are dietary strategies for cancer prevention that emphasize the consumption of low-energy density vegetables and fruit. The California Dept. of Health Services works with behavioral scientists, health professionals, and the private sector to improve nutrition and health status of the public.

Relative to Fischer 344 rats, Lewis rats demonstrate greater successive negative contrast and reduced effects of CDP on recovery from the loss of reward and on appetite. C.S. FREET, J.D. TESCHE, D.A. TOMPERS, K.E. RIEGEL, P.S. GRIGSON, *Dept. of Behavioral Science, Penn State University College of Medicine, Hershey, PA 17033, USA.*

Rats shifted from 1.0 M to 0.1 M sucrose consume less 0.1 M sucrose than controls that have only experienced the 0.1 M sucrose. This reduction in intake of the lesser reward is referred to as a successive negative contrast effect. Since Lewis rats show greater anticipatory contrast effects than Fischer rats, Experiment 1 was designed to determine whether Lewis rats also would demonstrate greater successive negative contrast effects. Half of the

Lewis and Fischer rats were given 5 minutes access to 0.1 M sucrose for 14 days. The other half were given 5 minutes access to 1.0 M sucrose for days 1-10 and then downshifted to 0.1 M sucrose for days 11-14. The results showed that Lewis rats exhibited a greater successive negative contrast effect, i.e., they consumed less of the 0.1 M sucrose than the unshifted controls and they recovered from contrast more slowly. Pretreatment with the anxiolytic agent chlordiazepoxide (CDP) delayed recovery from contrast in the Lewis rats, but facilitated recovery from loss of reward in the Fischer rats. In an attempt to test the appetite-stimulating effects of CDP, Experiment 2 examined the effects of CDP on intake of 0.1 M sucrose. The results showed that Fischer, but not Lewis, rats increased intake of sucrose following the CDP injection. Taken together, the results indicate that Lewis rats are more sensitive to the loss of expected reward, but are less sensitive to the anxiolytic and appetite-stimulating effects of CDP relative to Fischer rats. Supported by DA 09815 and DA 12473.

The food environment and food choices. S. FRENCH, *Department of Epidemiology, University of Minnesota, Minneapolis, MN 55454-1015, USA*

Environmental influences on eating and physical activity include changes in the food supply, eating away from home, and the effects of advertising, promotion, and pricing on eating habits. Public health efforts to influence population food choices include media campaigns, food packaging and labeling guidelines, and other policies that affect the economics of food choice. Experimental studies show that increasing the availability and decreasing the prices of low-fat food choices positively influences purchase and consumption patterns. Data from population based surveys and food disappearance measures show that advertising and marketing of healthful foods may lead to increased availability of the targeted foods in the food supply, resulting in increased consumption. The food industry is a key partner in developing and implementing strategies to influence population eating behaviors. Efforts are needed in the areas of food marketing and advertising, packaging, labeling, and pricing. Ideas include the "eat less" message; smaller package sizes; health labels on a wider variety of foods; labeling of restaurant and ready-made grocery store foods; and removal of price incentives for larger portion sizes of foods high in fat or added sugars. Food industry strategies to modify the food environment need to consider health issues, consumer desires, as well as corporate profits. Public health strategies and interventions aim for behavior change at the community level.

The effect of cocaine on consummatory and instrumental responding in rats. R.I. GEDDES, P.S. GRIGSON, *Dept. of Behavioral Science, Penn State University, College of Medicine, Hershey, PA 17033, USA.*

Rats suppress intake of a saccharin conditioned stimulus (CS) when followed by access to cocaine. This study aims to determine if this reduction is correlated with an increase in instrumental responding. Naïve adult male Sprague-Dawley rats (n=24) were given 5 min access to 0.15% saccharin adulterated with either Orange or Grape flavored Kool-Aid in the start box of a runway. Rats then had 15 min to traverse the runway at which time they were removed and subcutaneously (sc) injected with saline or cocaine (10 mg/kg). Dependent measures included: the latency to lick the CS, total licks elicited for the CS, and (3) the latency to traverse the runway. A 2 x 5 within-subjects ANOVA revealed differences in latency to lick and total CS intake, but not in runway speed. The latency to initiate CS licking was longer when the CS preceded cocaine rather than saline, $F(1,20) = 13.5$, $p<.001$. Analysis of total CS intake revealed a significant main effect of drug, $F(1,20) = 24.3$, $p<.001$, and trial, $F(4,80) = 29.97$, $p < .001$, as well as Drug x Trial interaction, $F(4,80) = 14.24$, $p <.001$. Post-hoc tests showed that CS intake was lower when predicting cocaine by trial 4, $p <.05$. Surprisingly, the nature of the drug injection did not have a significant effect on running speed ($Fs < 1$). Despite the failure to detect differences in running speed, the intake data demonstrate that rats can distinguish between the CSs and can use this information to predict cocaine reward. This research is supported by DA 09815 and DA 12473.

Cortisol following a stress test and dexamethasone suppression test (DST) in relation to psychopathology in the night eating syndrome. A. GELIEBTER, M.E. GLUCK, E. YAHAV, *New York Obesity Research Center. St. Luke's/Roosevelt Hospital, Columbia University College of Physicians & Surgeons, New York, NY 10025, USA.*

The Night Eating Syndrome (NES), described by Stunkard et al (1996) comprises morning anorexia, evening hyperphagia, and insomnia. Because HPA axis hyperactivity and exaggerated stress responses have been observed in other eating disorders, we examined cortisol baseline and cortisol stress response and DST in NES. There were 24 overweight women, BMI = 36.0 ± 5.0, age = 28.5 ± 7.1, body fat = 44.5% ± 5, which did not differ between groups (10 NES, 14 non-NES). Psychological scales included depression, global stress, and self-esteem. Participants underwent a cold stress test (CPT) at 12 noon, with the non-dominant hand in ice water for

2 min. Blood was drawn at -10, 0, 5, 15, 30, 45, 60 min. Baseline cortisol was greater (p = .03) in NES and rose significantly more (p =.006) following CPT. On another day, cortisol levels at 8 am, following 1 mg dexamethasone (DST) at 11 pm, did not differ (p =.36, ns) for NES. However, those with NES had more depression (p = .003), more global stress (trend, p =.055), and lower self-esteem (p = .03). Additionally, depression was correlated with the rise in cortisol (p = .008) and cortisol after DST (p = 046), but not with cortisol baseline (p = .74, ns). After controlling for depression, the higher cortisol baseline in NES lost significance (p = .14), but NES now had higher cortisol after DST (p =.03). In conclusion, NES is a syndrome with distinct HPA axis pathophysiology and associated psychopathology. Although some of the cortisol findings may be from associated depression, failure to suppress cortisol appears independently due to NES. Supported by NIH Grant DK 54318

Recognition of essential amino acid availability: the view from the anterior piriform cortex. D.W. GIETZEN, J.W. SHARP, T.J. KOEHNLE, J.A. BARRETT, B.G. TRUONG, *Dept. of Anatomy, Physiology and Cell Biology, School of Veterinary Medicine, Univ. Calif. Davis, Davis, CA 95616, USA.*

Essential (indispensable) amino acids (IAA), either in excess or deficiency, provide neural signals to the brain so that the organism can make appropriate adaptations for maintenance of protein synthesis. Rats alter their rate of eating (in mg/sec) within 15 min of introduction of an IAA deficient or imbalanced diet (IMB). The anterior piriform cortex (APC) is necessary for these responses. Several neurotransmitter and second messenger signaling pathways in the APC are involved, and have been seen in vivo and in vitro in response to IAA deficiency. Consumption of IMB activates APC neurons and initiates signaling that results in the early behavioral rejection of the IMB, followed by conditioned taste aversions and changes in gene expression (by 2 h). The initial signal by which depletion of an IAA is recognized has been shown to include activation of glutamate signaling, AMPA receptor activation and glutamine transporter activity. An early (<10 min) influx of calcium leads to activation of the CaMK and MAPK pathways. We hypothesize that these signals are involved in the earliest behavioral responses, and the later gene expression, which includes transcription of genes involved in: the activities of the glutamate, GABA and catecholamine transmitters; second messengers; changes in cytoskeletal elements, transporters and potassium and calcium channels. Taken together, the signaling and changes in transcription are all consistent with prior neuronal activation in the APC and increased glutamatergic output from its pyramidal cells for activation of feeding and conditioning pathways. Supported by NIH: NS33347, DK35747 and USDA: 2000-01049.

Obese binge eaters have a greater waist-hip-ratio (WHR), related to greater cortisol stress responsivity and hunger as compared to obese non-binge eaters. M.E. GLUCK, A. GELIEBTER, E. YAHAV, J. HUNG, *New York Obesity Research Center. St. Luke's/Roosevelt Hospital, Columbia University College of Physicians & Surgeons, New York, NJ 10025, USA.*

Higher cortisol levels and vulnerability to stress are related to central body fat and to food intake following a laboratory stress. We predicted obese bingers would have greater WHR, higher cortisol responsivity, and greater hunger following a stress test, compared to obese non-bingers. Thirty-one overweight women (BMI = 35.6 + 5.4 [SD], WHR = .88 + 7.6) were assessed for binge eating (18 bingers, 13 non-bingers). During the cold stress test (CPT), participants immersed their hand in ice water for 2 min. At 0, 2, 5, 15, 30, 45, and 60 min, ratings were made of hunger and desire to binge, and blood was drawn and assayed for cortisol. Age and BMI were similar across groups, but bingers had greater WHR (p = .02) than non-bingers. Basal cortisol was similar between groups but higher in bingers at 15 (p = .05) and 30 min (p = .04). Compared to non-bingers, bingers showed heightened cortisol responsivity with a trend for greater AUC (p = .07). WHR correlated with AUC (p = .02), and cortisol at baseline (p =.04), 15 (p =.01), and 30 (p =.09) min. Hunger increased in bingers at 45 (p = .03) and 60 min (p = .02), and desire to binge was greater at 15 (p = .03) and 60 min. (p = .05) compared to non-bingers. Results support a relationship between cortisol stress responsivity and WHR, suggesting the rise in cortisol might lead to increased hunger and binge eating. NIH DK54318 (AG); training grant (MG) DK07559.

Taste and Stress-Induced Eating Changes. J.H. GOLDBERG[1], S.J. KINGSTON[2], E.S. EPEL[3], K.B. HORGEN[2], M.A. NAPOLITANO[4], K.D. BROWNELL[2], *[1]Stanford Center for Research in Disease Prevention, Stanford University School of Medicine, [2]Department of Psychology, Yale University, [3]Department of Psychiatry, UCSF and [4]Department of Psychiatry and Human Behavior, Brown Medical School, Providence, RI, USA.*

While some individuals report increased eating under stress, others report decreased eating under stress. This study tested the hypothesis that changes in taste preferences and taste perceptions in response to stress are

associated with these two different eating patterns. Participants were thirty-nine male and female students (49% female; 64% Caucasian, 18% African American, 15% Asian; 21 ± 6 years of age) who reported eating more than usual (stress eaters, n=20) or less than usual (stress non-eaters, n=19) (group) under stress. Participants tasted and rated sixteen solutions varying in fat and sugar content under both stress and neutral conditions (condition). For men, there was a significant group by condition effect on taste preferences. Male stress eaters reported significantly greater taste preferences for the fat and sugar solutions under stress than in the neutral condition. Male stress non-eaters' taste preferences did not change between the two conditions. In addition, male stress eaters rated the solutions as more fatty in the stress condition than the neutral condition, whereas male stress non-eaters rated the solutions as less fatty in the stress condition than the neutral condition. For women, there was no apparent effect of stress on taste preferences or taste perceptions. These findings suggest that for male stress eaters, stress is associated with an increase in the enjoyment of fat and sugar and an increase in perception of fat.

Comparison of CNS infusion of melanocortin nonselective and –4 receptor selective agonists on energy balance in rats. J.N. GORSKI, G.J. HICKEY, A.M. STRACK, J. METZGER, *Dept. of Pharmacology, Merck Research Laboratories; Rahway, NJ 07065, USA.*

Central or peripheral administration of the nonselective melanocortin agonist, MTII, decreases food intake and body weight in rodents. We compare the effects of continuous central infusion of MTII with tetrahydroisoquinoline (THIQ1), a selective melanocortin 4 (MC4) receptor agonist on food intake, body weight and composition in male rats. 10-week old ad lib fed rats were infused by osmotic pump with vehicle, MTII (2 nmol/day) or THIQ1 (40 or 400 nmol/day) for twelve days. All groups decreased feeding due to operational stress on day 1. MTII administration significantly inhibited food intake on day 2 (44%) which was maintained (~18%) throughout the study. This was accompanied by a significant decrease in body weight evident from day 3 to day 12. DEXAscan analyses revealed the body weight loss was primarily fat mass (26% decrease), with no loss of lean mass. THIQ1 administration evoked a dose-related decrease in food intake (24 and 31%, respectively) on day 2 and a modest, nonsignificant suppression of food intake (6 and 13%, respectively) that was maintained throughout. THIQ1 administration resulted in no significant weight loss, however, the high dose group significantly decreased fat (~17%), but not lean mass. Although MTII and THIQ1 initially suppressed food intake, only MTII elicited sustained body weight loss, whereas MTII and high dose THIQ1 decreased fat mass. The divergent profile of action of MTII and THIQ1 on body weight might suggest a role for other MCR, most probably MC3R, in the CNS regulation of energy balance. Research supported by Merck & Co.

Quantitative analysis of ingestive behavior patterns in 5-HT2c receptor, obese, and agouti mutant mice. E.H. GOULDING, P. JUNEJA, J. WADE, L.H. TECOTT, *Dept. of Psychiatry, University of California, San Francisco, CA 94143, USA.*

To assess the impact of mutations that alter energy balance on behavior, a continuous home cage behavioral monitoring system for mice has been developed that measures food and water intake, as well as movement and position, with a high temporal resolution. Using this system, the patterns of ingestion and activity exhibited by 5-HT2C receptor null mutant, as well as obese and agouti mutant mice, have been quantitatively classified. Both wild type and mutant mice exhibit a pattern of ingestion characterized by bouts of feeding intermixed with bouts of drinking and activity. These bouts cluster together in time, and the duration and size of these clusters varies with both circadian cycle and genotype. The 5-HT2CR mutant mice exhibit hyperphagia solely during the light cycle, and this hyperphagia results from an increase in the number of clusters with a concordant decrease in intercluster interval compared to wild type mice. While the 5-HT2CR mutant mice do not exhibit hyperphagia during the dark cycle, their pattern of ingestion is altered with an increase in the number of clusters accompanied by a decrease in cluster size such that dark cycle intake is similar to that of wild type mice. Both the obese and agouti mutants exhibit hyperphagia during the light and dark cycle with an increase in cluster size that is also accompanied by an increase in intercluster interval compared with wild type mice. These distinct patterns of ingestion can be interpreted as indicating different roles for these mutations in altering satiation and satiety.

Postnatal ontogeny of arcuate nucleus neuropeptide Y (NPY) projections to orexin and melanin-concentrating hormone (MCH) neurons in the lateral hypothalamic area (LHA), B. GRAYSON, S. ALLEN, M.S. SMITH, K.L. GROVE, *Division of Neuroscience, Oregon National Primate Research Center, Oregon Health & Science University, Beaverton, OR 97006, USA.*

NPY neurons in the arcuate nucleus (ARH) are potent orexigenic stimuli due to their projections to important hypothalamic feeding centers, such as the paraventricular nucleus (PVH) and LHA. They also exclusively

colocalize with AGRP, making AGRP an excellent marker for ARH-NPY neurons. Our studies show that direct projections of ARH-NPY/ AGRP neurons to the PVH do not develop until after the second postnatal week. However, before direct connections are made, the PVH may be indirectly modulated by ARH-NPY/AGRP neurons via pathways to the LHA, with MCH and orexin neurons being the conduit neurons to the PVH. In this study we first characterized the temporal development of ARH-NPY/AGRP projections to the LHA, using fluorescent immunohistochemistry coupled with confocal microscopy. Although MCH neuronal projections to PVH were developed by postnatal day 2 (P2), NPY/AGRP fibers in the LHA were not evident at P2 and did not become abundant until P10-11. Thus, from P2-P10, mostly single-label NPY fibers made close contacts with MCH neurons. We detected only lightly stained orexin cell bodies commencing at P6, but. by P10-11, an abundance of ARH-NPY/AGRP contacts orexin cells were present. In addition, we showed that the NPY Y1 receptor was not colocalized with MCH or orexin cells, although Y1-ir fibers were observed contacting both types of cells, suggesting a presynpatic action of NPY. In conclusion, prior to the development of direct ARH-NPY projections to the PVH, NPY neurons of an unknown source provide input into MCH neurons that may in turn modulate PVH neuronal activity.

Normalization of delayed gastric emptying after treatment for bulimia nervosa. J.L. GUSS, B.T. WALSH, H.R. KISSILEFF, E. ZIMMERLI, R. SYSKO, M.J. DEVLIN, *Obesity Research Center & Columbia University, New York, NY 10025, USA.*

This study was undertaken to compare gastric emptying (GE) between women with (n=16) and without (n=16) bulimia nervosa (BN) and, among patients (n=9), before and after they successfully completed treatment for BN (i.e., cessation of binge/purge activity for >4 weeks). GE of 99mTc DTPA-labeled Ensure Plus (EP) (1.5 kcal/g, 600g) was monitored via gamma scintigraphy for 90 min. Before treatment, patients retained significantly more EP (400g ± 9.5 SE) than controls (288g ± 16.4 SE; $t = 5.96$, $p = 0.0001$) after 90 min. After completing treatment, 14.5% more (± 3.5 SE) EP had emptied after 90 min compared to pre-treatment (paired $t = 4.14$, $p = 0.014$). Before treatment, GE rate was 1.3 g/min slower (± 0.20 SED) for patients with BN (2.3 g/min ± 0.10 SE) than for controls (3.6 g/min ± 0.18 SE; $t = 5.96$, $p = 0.0001$), but after treatment, GE rate increased significantly (by 1.0 g/min ± 0.24 SED; $t = 4.14$, $p = 0.01$). Patients, therefore, exhibited a reduced rate of GE which improved significantly after termination of binge/purge activity. This finding suggests that observed delays in GE among patients with BN may be a state-related phenomenon that remits with recovery. Since gastrointestinal feedback plays a critical role in satiation, rapid normalization of disturbed GE in these patients may mediate, or be indicative of, a return to normalized feeding responses. Supported by NIMH Predoctoral Training Grant MH12901, MH42206, and the NY Obesity Research Ctr.

Chronic changes in body weight of rats exposed to acute stress. R.B.S. HARRIS, J. ZHOU, D.H. RYAN, *University of Georgia, Athens, GA 30602 and Pennington Biomedical Research Center, Baton Rouge, LA 70808, USA.*

It is well established that stress inhibits food intake and weight gain. Rats exposed to 3 hours restraint stress on 3 consecutive days (repeated restraint) are hypophagic and lose 5 to 10% body weight. Food intake returns to normal post-stress, but body weight does not return to that of non-stressed controls for periods as long as three months. Weight loss during restraint is lean tissue but fat is lost during immediately following stress and is associated with a temporary increase in the number of adipocyte b-adrenergic receptors. Weight loss is exaggerated by a second bout of restraint but not by increasing the number of days included in one bout of repeated restraint. Rats that are food restricted or overeating on the days of restraint return to a lower body weight than non-stressed controls when ad libitum feeding is restored. Thus, repeated exposure to acute stress initiates a cascade of events that causes a chronic down-regulation of body weight. Central pathways responsible for this weight loss have not been identified. Activation of CRF receptors in the hypothalamus initiates the response, but there is no evidence of chronic activation of this system. Mice that over-express agouti protein show an exaggerated stress response, suggesting that the melanocortin system normally antagonizes the weight loss. Thus, repeated restraint stress provides a unique model for investigating mechanisms that regulate body weight and for determining how these pathways are disrupted by stress. Supported by US Army Grant DAMD 17-97-2-7013

Low circulating adiponectin levels and reduced adipocyte adiponectin production in obese, insulin-resistant sprague-Dawley rats. P.J. HAVEL, J. GRAHAM, K.L. STANHOPE, *Dept. of Nutrition, University of California, Davis, CA 95616, USA.*

Inbred Sprague-Dawley rats from Charles River (CRSD) are heavier and have elevated insulin and leptin concentrations compared to rats from Harlan Sprague-Dawley (HSD), even when consuming a low-fat diet. Insulin-stimulated glucose utilization is decreased in isolated adipocytes from CRSD (Obesity Res., 2000). Adiponectin is an adipocyte protein reported to improve insulin sensitivity in insulin-resistant rodents. To investigate the potential role of adiponectin in differences in insulin sensitivity between CRSD and HSD, we compared circulating adiponectin levels and adiponectin production from cultured adipocytes, as well as body weight, adiposity, food intake, glucose and insulin in CRSD (n=13) and HSD (n=9) rats from 2 to 16 months of age. CRSD rats were hyperphagic at 2 (28.9±1.0 vs 23.5±0.9 g/d, $p<0.001$) and 16 months (36.7±1.2 vs 27.0±0.8 g/d, $p<0.0001$). By 16 months the CRSD were 50% heavier (813±30 vs 561±13 g, $p<0.0001$) and had a higher percent body fat measured by DEXA (29.0±1.5 vs 12.5±1.1 $p<0.0001$) Weight gain per amount of food consumed revealed that the CRSD rats are nearly twice as metabolically efficient (165±9 vs 296±24 kcal/g, $p<0.0001$). At 3 months the CRSD had lower plasma adiponectin levels (4.8±0.4 vs 7.6±0.7ug/ml, $p<0.01$) and cultured adipocytes from CRSD rats secreted less adiponectin (179±12 vs 223±10 ng/ml, $p<0.01$). At 11 months, plasma adiponectin remained lower in the CRSD (4.9±0.3 vs 7.0 ± 0.6 ug/ml, $p< 0.001$). In conclusion, the inbred CRSD rat is novel animal model of adult-onset obesity and insulin resistance. Reduced adiponectin production may contribute to the onset of the insulin resistance.

Leptin´s role in anorexia nervosa. J. HEBEBRAND, C. EXNER, M. KLINGENSPOR, H. REMSCHMIDT, *Clinical Research Group, Dept. of Child and Adolescent Psychiatry, Philipps-University of Marburg, 35039 Marburg, Germany.*

Leptin is a hormone synthesized in fat cells that signals the size of the adipose tissue to the brain. In the light of leptin´s role in the physiological adaptation to semi-starvation it is of obvious interest to assess the somatic and behavioral implications of the hypoleptinemia associated with acute anorexia nervosa (AN). Longitudinal endocrine studies in both female and male patients indicate that threshold levels of circulating leptin are required for normalisation of the hypothalamic-pituitary-gonadal axis. To assess a potential role of leptin in the hyperactivity commonly observed in patients with AN, we investigated semistarvation induced hyperactivity (SIH) in rodents. Rats, which had established a stable level of activity, were treated with leptin or vehicle via implanted minipumps concomitantly to initiation of food restriction for 7 days. In a second experiment treatment was initiated after SIH had already set in. In contrast to the vehicle-treated rats, which increased their baseline activity level by 300%, the development of SIH was suppressed by leptin. Furthermore, leptin was able to stop SIH, after it had set in. In parallel to these experiments we assessed subjective ratings of motor restlessness in 30 patients with AN in the emaciated state and after increments in leptin secretion. Hypoleptinemic patients ranked their motor restlessness higher than upon attainment of their maximal leptin level during inpatient treatment. The results underscore the assumed major role of leptin in the adaptation to semi-starvation. Hypoleptinemia might contribute to the hyperactivity frequently associated with AN.

Glutamate is released in the lateral hypothalamus during meal initiation, whereas release of GABA, in relation to glutamate, corresponds with satiation: simultaneous 30-sec measurements in the rat. L. HERNANDEZ, B.G. HOEBEL, A. MENDIALDUA, P. RADA, *Princeton University, NJ 08544-1010, USA and University of Los Andes, Venezuela.*

It is known that lateral hypothalamic injections of glutamate can initiate eating, and GABA can stop the meal. This suggests that glutamate inputs are active at the beginning of a meal, and GABA might be released at the meal's end. To test this hypothesis, microdialysis was used to sample glutamate and GABA simultaneously every 30-sec during a meal. Samples were tagged with fluorescein, and then capillary electrophoresis was used to separate the amino acids for quantitative detection of laser-induced fluorescence. Male rats (N=8) were deprived of food for 16 hours, then given chow. The result was a significant increase in extracellular glutamate that peaked during the first third of the meal (169% of baseline), then glutamate gradually decreased to below baseline while the animals were still eating (72% of baseline). GABA, on the other hand, increased early in the meal (133%) and continued rising to a maximum during the last third of the meal (160%). GABA remained high when the animals were satiated. In light of local injection studies that give causative effects, the present correlations between neurotransmitter release and behavior lead to the conclusion that glutamate inputs to the lateral hypothalamus create appetite in animals that are physiologically ready to eat, and GABA input contributes to satiation. Supported by USPHS grant DA10608 (to BGH), CONICIT G-97000820 9 (to LH) and CDCHT-ULA M-661-99-03-A (to PR).

Microstructural analysis of the effect of exogenous and endogenous cannabinoids on licking for sucrose. S. HIGGS[1], [2]C.M. WILLIAMS, T.C. KIRKHAM[2]. [1]School of Psychology, University of

Birmingham, Edgbaston, Birmingham, B15 2TT, UK, [2]*Dept. of Psychology, University of Reading, Earley Gate, Reading, RG6 6AL, UK.*

Although central cannabinoids have been implicated in appetite control, the motivational changes underlying the respective hyperphagic and anorectic actions of CB1 agonists and antagonists remain to be determined. Possible influences of cannabinoids on palatability were investigated by examining the effects of both exogenous and endogenous agonists, and a CB1 receptor antagonist, on licking behaviour in the rat. Microstructural analyses of licking for a palatable 10% sucrose solution were performed over a range of drug doses administered to non-deprived male rats. Delta-9-THC (0.5, 1 and 3 mg/kg) and anandamide (1 and 3 mg/kg) significantly increased total number of licks in 30 min. This was primarily due to an increase in bout duration rather than bout number. There was a non-significant trend toward an increase in total licks following administration of 2-arachidonoyl glycerol (0.2, 1.0 and 2 mg/kg), whereas administration of the cannabinoid receptor antagonist SR141716 (1 and 3 mg/kg) brought about a significant decrease in total licks. All drugs (with the exception of anandamide) significantly decreased the intrabout lick rate. An exponential function was fitted to cumulative lick rate curves for each drug. This analysis showed that all compounds altered the asymptote of this function without having any marked effects on the exponent. These data are consistent with an action of cannabinoids to enhance palatability.

Effects of nicotine on the behavioral satiety sequence in outbred mice. S. HIGGS[1], R. HALAMANDRES[2], A.J. COOPER[2], [1]*School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK,* [2]*Dept of Pharmacology, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK.*

The behavioural mechanisms underlying the anorectic effect of nicotine remain to be identified. In this study, non-deprived male CD1 mice were habituated to daily presentation of a sweet wet mash. Following familiarisation, nicotine (0.5-2 mg/kg s.c.) was administered acutely, 30 min prior to diet presentation. Behavioural satiety sequence measures were taken for the subsequent 40 min, and food intake recorded. Nicotine did not significantly affect consumption of the mash, although there was a tendency for intake to be increased at the 0.5 and 1 mg/kg doses and reduced at the highest dose (2 mg/kg). Ingestion of the mash in vehicle treated mice did not result in the development of a typical satiety sequence. The incidence of feeding declined over the test session, but there were no clear changes in activity or grooming. Resting behaviour increased as the session progressed but levels of resting never constituted a large percentage of the total observations. The principal effects of nicotine were to decrease activity (drug x time interaction: $P < 0.05$), and increase resting (drug x time interaction: $P < 0.01$) in the early part of the test, suggesting that the drug disrupted behaviour non-specifically. These data indicate that in naive mice, relatively low doses of nicotine may not decrease short-term feeding behaviour, but can cause a generalised behavioural impairment. This may have implications for studies examining the anorectic effect of nicotine in both acute and chronic studies.

Antagonism of cocaine-induced hypophagia by the a1-adrenoceptor antagonist prazosin in the rat. D.H. HO, P.J. WELLMAN, J.R. NATION, L. BELLINGER, *Psychology Dept., Texas A&M University, College Station, TX 77843-4235, USA.*

Cocaine inhibits eating in rats, an action that may reflect activation of alpha1-adrenoceptors (ADRs) consequent to antagonism by cocaine of the norepinephrine transporter. In the first study, consumption of a sweetened-mash diet and of tap water was monitored for 60 min in rats pretreated with prazosin (0, 1, or 2 mg/kg, IP) and then treated (IP) with 0, 10, 20 or 40 mg/kg (IP) cocaine, whereas a second study examined the impact of prazosin (0, 0.5, or 2 mg/kg, IP) and cocaine (0, 10, 20 or 40 mg/kg, IP) on several indices of locomotion in rats (total distance traveled scores or stereotypy counts) assessed in automated activity monitors. Administration of prazosin alone (in the absence of cocaine) did not alter baseline food intakes, water intakes or either measure of locomotion. Pretreatment with prazosin significantly attenuated the hypophagic action of 20 mg/kg cocaine ($p < 0.04$), but not 40 mg/kg cocaine. A similar pattern was noted for the impact of prazosin on cocaine-induced increases in total distance traveled scores as well as for stereotypy counts. These findings suggest that activation of alpha1-ADRs contributes to the hypophagic actions of cocaine and extends earlier studies in which prazosin administration in rats attenuates the hypophagic properties of aminorex, amphetamine, ephedrine, phenylpropanolamine, phentermine, and sibutramine.

Hypothalamic galanin in relation to alcohol intake and dopaminergic motivation. B.G. HOEBEL, S.F. LEIBOWITZ, *Princeton University, USA; Rockefeller University, NJ 08544-1010, USA.*

RATIONALE. Galanin (GAL) injection in the paraventricular nucleus (PVN), like systemic alcohol, can alter dopamine/acetylcholine balance in the nucleus accumbens (NAc), suggesting that endogenous GAL expression might respond to alcohol. METHODS. Exp. 1: Male Sprague-Dawley rats were injected with saline or alcohol (5 days, 0.8 gm/kg i.p. 10% v/v alcohol, N=10/group), then food deprived for 3 hrs and brains were analyzed using in situ hybridization and immunocytochemisty. Exp. 2: Male and female rats (N=10 each) were given ad lib chow, water and alcohol that was gradually increased from 1% to 9% v/v. The 5 rats/group exhibiting the greatest alcohol consumption, and control animals drinking only water, were similarly analyzed. RESULTS. Males and females given alcohol i.p., or allowed to drink voluntarily, showed significantly elevated GAL mRNA ($p<0.05$) and GAL-ir in the dorsomedial nucleus (DMN), anterior-PVN and a similar trend in the perifornical lateral hypothalamus. Neuropeptide Y (NPY) showed reduced expression in the arcuate nucleus. DISCUSSION. 1) Ethanol injection markedly increases the expression of GAL, but not NPY, in specific nuclei of the hypothalamus. 2) Rats can be induced to drink ad libitum alcohol voluntarily without adding any sugar or flavoring. 3) Voluntary intake of alcohol also stimulates GAL expression. 4) GAL injected into the PVN stimulates dopamine (DA) release in the nucleus accumbens (NAc), linking GAL to the addiction process. Supported by Lane Foundation and USPHS grant AA-12882.

Hepatic branch vagal afferent fibers are directly sensitive to 5-HT and contain 5-HT3 receptors. C.C. HORN, M.I. FRIEDMAN, *Monell Chemical Senses Center, Philadelphia, PA 19104, USA*.

Peripheral 5-HT is implicated in the physiology of emesis, nausea, gut motility, and feeding. The common hepatic branch (CHB) of the vagus innervates intestinal, gastric, and hepatic sites and is in a prime position to detect nutrients and toxins. Using electrophysiology we investigated the 5-HT sensitivity of common hepatic branch (CHB) vagal afferent fibers. Twenty-eight single units were isolated from the CHB of nine rats. 79% of the units were sensitive to 5-HT (10 micrograms), and 27% of these were also sensitive to CCK-8 (100 pMol). 73% of the 5-HT sensitive units had a larger response when 5-HT was infused into the jugular vein than into the portal vein. A 5-HT3-receptor antagonist (Y-25130) blocked the effect of 5-HT on CHB activation. Combined treatment with atropine and pancuronium, which inhibit gut peristalsis, did not affect the 5-HT response. The results suggest that most of the CHB 5-HT sensitive units do not innervate the portal vein or liver but instead innervate the GI tract, and that these afferent fibers contain 5-HT3 receptors. Supported by NIH grants DK02894 and DK36339.

Feature clustering as a tool for the analysis of single-unit vagal afferent activity. C.C. HORN, M.I. FRIEDMAN, *Monell Chemical Senses Center, Philadelphia, PA 19104, USA.*

A system for recording electrophysiological signals from single afferent vagal fibers in the anesthetized rat is presented. To determine the stimulus coding properties of gastrointestinal and hepatic sensory neurons that provide input to the brain we have utilized methods for recording single-unit afferent responses from the subdiaphragmatic vagus nerve. We used feature detection analysis and cluster cutting to analyze the simultaneous activity of up to four single units from each nerve filament. To increase data acquisition we also recorded the responses of several nerve filaments at once using an array of electrodes. Due to recording instability caused by respiratory movements it is typically difficult to isolate the activity of single subdiaphragmatic vagal nerve fibers. Instability was effectively reduced by mechanical ventilation with the administration of a paralytic agent and by using feature detection analysis to assess waveform variability. Supported by NIH grants DK02894 and DK36339.

Magnetic field exposure decreases ad lib drinking by increasing latency. T.A. HOUPT, B.S. KWON, J.A. CASSELL, C. RICARDI, J. SMITH, *Dept. Biological Science, The Florida State University, Tallahassee, FL 32306-4340, USA*

Static magnetic fields are commonly used in MRI machines, but the physiological effects on mammals are largely uncharacterized. We have found that exposure to high strength static magnetic fields (e.g. 7 T and above) induces conditioned taste aversion, circular locomotion, and c-Fos in brainstem visceral and vestibular nuclei. Here we examined the acute effects of high strength magnetic fields on ingestive behavior. Water-deprived rats were restrained in plastic tubes and inserted into the core of a 14T superconducting NMR magnet for 0, 5, 10 or 30 min, or sham-exposed for 30 min. Immediately after exposure, the rats were returned to their home cages and given 10-min access to a 3% glucose, 0.125% saccharin solution (G+S) from an overhead bottle. Sham rats consumed 10 ml or more with very short latency, but rats exposed to the magnetic field for 5 min or longer showed significantly longer latency and lower intake. When rats were allowed to drink for 10 min after their first lick (i.e. when latency was controlled for) there was no significant difference in intake between magnet- and

sham-exposed rats. Furthermore, when rats were exposed prior to a 10 ml/10 min intraoral infusion of G+S, intake was identical in both magnet- and sham-exposed groups. These results are consistent with the suppression of drinking induced by vestibular stimulation; because latency to drink from overhead bottles was increased, we hypothesize that a vestibular perturbation induced by the magnetic field suppresses the postural changes required for ad lib drinking. Supported by NIDCD04607.

Prostaglandin E2 may act at the raphe nucleus to mediate the anorexia following peripheral lipopolysaccharide administration. B.J. HRUPKA, W. LANGHANS, *Institute of Animal Sciences, Swiss Federal Institute of Technology, 8603 Schwerzenbach, Switzerland.*

Both prostaglandins and serotonin play a role in lipopolysaccharide (LPS)-induced anorexia in the rat. Because serotonergic neurons in the raphe nucleus contain prostaglandin E2 (PGE2) receptors, we assessed whether PGE2 may act there to modulate the anorexia following LPS. Raphe injections were performed at dark onset through two guide cannulae aimed at the dorsal and medial raphe nucleus. In Exp. 1&2, PGE2 was administered to 16 hr food-deprived rats. In Exp. 1, 100 ng PGE2 was injected into both the dorsal and medial raphe in rats trained to eat a sweetened chow mash. PGE2-injected rats ate significantly less than control rats (20 min intake, 13.4±0.7 vs. 23.1±1.7 g respectively, $P<0.001$). In Exp. 2, rats injected with 0, 1, 10 or 100 ng PGE2 into the dorsal raphe ate 3.6±0.7, 3.8±0.5, 1.4±0.4 and 2.0±0.3 g respectively (30-min chow intake). Food intake was reduced in rats injected with 10 ng ($P<0.05$), but not 1 ng PGE2. In Exp. 3, LPS-treated rats (100 µg/kg, IP) were injected with 0, 1 or 1000 ng of the cyclooxygenase-2 inhibitor NS-398 into the dorsal and medial raphe. Rats injected with 1 ng NS-398 ate nearly twice as much as control and 100 ng NS-398 rats by 4 hr ($P<0.05$). Our results indicate that PGE2 in the dorsal (and possibly medial) raphe reduces food intake in rats, and that inhibition of prostaglandin synthesis in the raphe nucleus following LPS can attenuate LPS-induced anorexia.

Subdiaphragmatic vagal deafferentation increases meal size in male Sprague-Dawley rats. B.J. HRUPKA[1], G.J. SCHWARTZ[2] and W. LANGHANS[1], [1]*Institute of Animal Sciences, Swiss Federal Institute of Technology, 8603 Schwerzenbach, Switzerland, and* [2]*NY-Hospital-Weill Cornell Medical College, White Plains, NY 10605, USA.*

To assess the role of extrinsic afferent innervation of the upper gut in food intake regulation, we measured meal patterns of solid food in rats following subdiaphragmatic vagal deafferentation (SDA) or after a combination of SDA and celiac superior mesenteric ganglionectomy (COM). Meal patterns were recorded for 5 days starting 2.5 weeks and 2.5 months after surgery. Intermeal interval was determined by breakpoint analysis for each rat. At both 2.5 weeks and 2.5 months, average dark-phase meal size was similar between SDA and COM rats, but was increased in both groups compared to control rats (all $P<0.05$). At 2.5 weeks, average dark-phase meal size was 3.1±0.1, 4.0±0.1, and 4.0±0.1g for control, SDA and COM rats respectively. Although meal size distribution was skewed, changes in median meal size reflected changes in mean meal size. Compared to control rats, the number of dark-phase meals was reduced in SDA and COM rats (7.7±0.4 vs. 6.1±0.2 and 6.6±0.3 meals/dark phase). At 2.5 months, average dark-phase meal size was 3.2±0.1, 4.1±0.1, and 3.7±0.1g for control, SDA and COM rats. At both 2.5 weeks and 2.5 months, the consumption of larger meals occurred primarily during the middle 6 hr of the dark phase ($P<0.05$). Meal size also tended to be increased during the first 3 hr of the dark phase, but not during the last 3 hr. These results are consistent with a role for gut vagal afferent negative feedback signals in the control of meal size.

Selective immunotoxin lesion of hindbrain norepinephrine (NE) and epinephrine (E) neurons impairs the consummatory feeding response to glucose deficit. B.D. HUDSON, S. RITTER, *Dept. of Veterinary and Comparative Anatomy, Pharmacology and Physiology, Washington State University, Pullman, WA 99164-6520, USA.*

A variety of evidence indicates that hindbrain NE/E neurons with projections to forebrain participate in the appetitive aspects of glucoprivic feeding. For example selective immunotoxin lesion of NE/E neurons abolishes glucoprivic feeding. However, Flynn and Grill (Science 221:188-190, 1983) demonstrated that glucoprivation increases the consummatory response to food placed in the mouth even when all neural connections between hindbrain and forebrain have been severed by supracollicular decerebration. Therefore, we examined the contribution of NE/E neurons to the consummatory feeding response to glucoprivation. NE/E neurons with projections to the forebrain were selectively lesioned by bilateral PVH injections of anti-dopamine-ß-hydroxylase conjugated to the ribosomal toxin, saporin (DSAP). Consummatory responses to 2DG (200 mg/kg), insulin (1.5 U/kg), and saline were subsequently tested by presenting 40% lactose-free milk through an intraoral cannula. Milk was infused at a constant rate until actively rejected. Controls consumed significantly more milk

after either insulin (36.2±2.3 ml) or 2DG (45.5±2.2 ml) than after saline (26.9±1.67 ml). DSAP rats did not increase their consumption above baseline (18.4±2.2 ml) to either challenge (18.8±1.6 ml and 16.5±2.2 ml). We also found no differences between control and DSAP rats in gastric emptying of sucrose or in 5 min intake of 3%, 7.5%, 15% and 30% sucrose that could account for the glucoprivic consumption deficit. Results indicate that NE/E neurons are required for both the appetitive and consummatory feeding responses to glucoprivation. The consummatory response may be mediated by hindbrain terminals of the same NE/E neurons that innervate hypothalamic sites where DSAP was injected.

Glucocorticoid receptor mediated down-regulation of nNOS in the rat PVN during food deprivation. J.W. JAHNG, Y.M. KIM, K.I. Park[1], *Dept. of Pharmacology, Pediatrics[1], and Yonsei Brain Research Institute, BK21 Project for Medical Science, Yonsei University College of Medicine, Seoul, 120-752, Korea.*

Nitric oxide (NO) is an important biological messenger, especially in the hypothalamic paraventricular nucleus (PVN) of the brain, NO modulates a large number of neuronal, autonomic, and endocrine functions. Expression of neuronal nitric oxide synthase (nNOS), the enzyme producing NO in the PVN, is down-regulated by fasting, and we previously reported that adrenalectomy abolishes fasting-induced down-regulation of PVN-nNOS and dexamethasone (DEX), a synthetic glucocorticoid, down-regulates the PVN-nNOS in intact rats. Also we found that refeeding-induced expression of the PVN-nNOS was blocked by DEX administration shortly before the onset of food. Recently, nNOS has been considered as an inducible gene, and our previous results suggest that changes in plasma glucocorticoids level according to different feeding conditions, such as fasting or refeeding, may negatively influence nNOS expression in the PVN, however, its molecular mechanism is not clear yet. In the present study, we examined if glucocorticoid antagonism would block the fasting-induced down-regulation of PVN-nNOS. RU486, glucocorticoid receptor antagonist, was subcutaneously injected twice daily during 48h food deprivation, and rats were transcardially perfused with 4% paraformaldehyde at 12h after the last injection, then the PVN sections were processed with NADPH-diaphorase staining, and the number of NADPH-d stained cells in the PVN was compared with vehicle injected group. In the result, NADPH-d cells in the PVN significantly decreased in vehicle group (~35% decrease), but not in RU486 group, during 48h food deprivation, compared to non-deprived control. This indicates that glucocorticoid receptors may mediate nNOS down-regulation in the PVN during food deprivation.

Differential hepatic energy status and food intake in genetically obese and lean rats and mice. H. JI, M.I. FRIEDMAN, *Monell Chemical Senses Center, Philadelphia, PA 19104, USA.*

Hepatic energy metabolism has been implicated in the control of food intake in rats such that a reduction in hepatic energy status (ATP content or phosphorylation potential) generates a signal that triggers eating behavior. Rats with experimental diabetes mellitus or ventromedial hypothalamus lesions have chronically lower hepatic energy status and are hyperphagic. In this study, we assessed hepatic energy metabolism and food intake in two genetically obese rodent models, the Zucker rat and the ob/ob mouse. Results showed that under fed conditions, obese rats and mice had reduced hepatic energy status compared with their lean littermates. When fasted, hepatic energy status in lean littermates decreased as expected, whereas in obese rats and mice it increased. Obese rats and mice ate more under ad libitum feeding conditions, but ate less during the first 30 min of refeeding after a 12-h fast than their respective lean controls. This early reduction in food intake during refeeding was reversed when obese mice consumed a small food preload (0.11 g) and when obese rats were pretreated with methyl palmoxirate, an inhibitor of fat oxidation. Hepatic ketone body content was increased by 150% by the fast and totally reversed by the preload in mice. These results suggest that hepatic energy metabolism plays a role in the control of food intake in Zucker rats and ob/ob mice. In obese rodents, hepatic energy status seems to be lowered by impaired fat oxidation; fat oxidation and energy status are enhanced by fasting. This work supported by NIH Grant DK-53109.

Hepatic energy metabolism in a mouse model of Prader-Willi syndrome. H. JI, M. STEFAN[1], J.L. KNEPPER[1], R.S. AHIMA[1], R.D. NICHOLLS[1], M.I. FRIEDMAN, *Monell Chemical Senses Center and [1]University of Pennsylvania, Philadelphia, PA 19104, USA.*

Prader-Willi syndrome (PWS) is caused by several genetic defects in paternal imprinted expression in chromosome 15q11-q13, including a 4 Mb chromosome deletion. PWS infants are hypotonic and fail to thrive with subsequent onset of hyperphagia and severe obesity. PWS mouse pups appear to be hypophagic with failure-to-thrive and numerous other physiological abnormalities including severe hypoglycemia, hypoinsulinemia, abnormal body composition, impaired oxygen consumption and thermogenesis, and usually do

not survive past 7 days postnatal. We examined hepatic energy status and circulating fat fuels in PWS transgenic deletion and wildtype (WT) pups in order to investigate whether abnormal energy metabolism contributes to the neonatal phenotype of PWS pups. Compared to WT pups, 3-day old PWS pups had 32% higher hepatic ATP content but similar ATP/ADP ratio and phosphorylation potential, and 74% higher hepatic ketone content. In addition, circulating free fatty acids, triglycerides and ketone bodies were 63% lower, 31% lower and 160% higher in PWS pups than in WT pups, respectively. These results indicate that PWS pups had normal or above normal hepatic energy status possibly caused by accelerated fat oxidation despite severe deficits in glucose and fat fuel supplies. They suggest that high hepatic energy status may contribute to the abnormal neonatal phenotype of the PWS mouse pups which seemingly affects fat and energy metabolism, and that severe ketoacidosis is likely one of the factors leading to neonatal mortality. This work is supported by NIH Grants DK-53109 and HD31491.

Price affects choice between pellets of sucrose and chow. D. JOHNSON, G. COLLIER, *Dept. of Psychology, Rutgers University, Piscataway, NJ 08854-8000, USA.*

The inclusion of pure carbohydrates in the diet depends on a number of factors, including the type of saccharide, its concentration and form, and, as we have shown, on its price. We investigated whether the form of sucrose (solid vs. solution) influenced how the price of sucrose affects rats' choices between sucrose and chow. Laboratory rats had continuous access to two feeders, one of sucrose pellets and one of chow pellets. Meals could occur on only one food at a time; rats could choose either feeder at the start of each meal and meals could be of any size. Each pellet cost a fixed number of bar presses. The rats ate less of each food as its pellet price increased, i.e., more sucrose when chow was expensive and more chow when sucrose was expensive; however, the trade-off was not symmetrical. The rats persisted in eating chow at higher prices than they were willing to pay for sucrose. Although solid sucrose is reported to be less palatable to rats than sucrose solution, these rats chose between chow and sucrose pellets in a manner comparable to that of rats working for chow pellets and sips of sucrose solution. Palatability factors appear to be less important than nutrient and cost factors in this choice.

Relative fat and carbohydrate intake is different for PROP tasters and non-tasters. M.M.J.W. KAMPHUIS, M.P.G.M. LEJEUNE, M.S. WESTERTERP-PLANTENGA, *Dept. of Human Biology, Maastricht University, The Netherlands.*

Sensitivity to the bitter taste of 6-n-propylthiouracil (PROP) is a heritable trait. The ability to taste PROP has long been associated with an enhanced sensitivity to sweet and bitter compounds(1) and recently with fat perception(2). However, the effect of PROP taster status on macronutrient selection hardly has been studied. The PROP-taster status of 36 subjects was identified as described before(3). An ad lib. lunch was offered to investigate difference in macronutrient selection between PROP tasters (PT) and PROP non-tasters (PNT). Hunger and satiety levels were measured before and after the lunch. Eleven women and 11 men were PT (medium and super tasters) while 11 women and 3 men were PNT. No differences in body weight, BMI, age or dietary restraint (F1 of TFEQ) between PT and PNT were seen, corrected for the different number of subjects. Hunger and satiety levels did not differ between PT and PNT. Moreover, there was no difference in amount eaten (gram and kJ). However, PT ate a higher percentage energy from fat than PNT (44.9±8.7% vs. 37.5±9.6%, $p<0.05$) and a lower percentage energy from carbohydrate (43.2±9.1% vs. 50.8±10.0%, $p<0.05$). There was no difference in protein intake. We conclude that PROP tasters compared to PROP non-tasters are more vulnerable to high fat foods from a mixed lunch. 1) Bartoshuk, Science, 1979; 205:934 2) Tepper and Nurse, Physiol. Behav., 1997; 61:949 3) Bartoshuk, Physiol. Behav., 1994; 56:1165

CLA affects resting metabolic rate, fat free mass and appetite, but not body weight regain, fat mass or energy intake. M.M.J.W. KAMPHUIS, M.P.G.M. LEJEUNE, M.S. WESTERTERP-PLANTENGA, *Dept. Human Biology, Maastricht University, The Netherlands.*

In animals, Conjugated Linoleic Acid (CLA) has been shown to reduce body fat and energy intakes and to increase lean body mass and energy expenditure. In humans, effects were found on fat mass or on sagital abdominal diameter, but not on weight loss. In this study, we investigated the effect of CLA after weight loss on body weight regain, changes in body composition, resting metabolic rate (RMR), energy intake at breakfast (EI) and parameters of appetite. Overweight, healthy non-smoking subjects (n=54) were first submitted to a VLCD (2.1 MJ/d) for 3 weeks after which they received 1.8g or 3.6g CLA (1.8g: n=14, 3.6g: n=13) or placebo (1.8g: n=13, 3.6g: n=14) per day for 13 weeks. Measurements were conducted before VLCD (t=-3), after VLCD but before CLA intervention (t=0) and at the end of the intervention (t=13). Multiple regression analysis showed that at t=13 CLA did not have an effect on body weight regain and fat mass, but did increase fat free mass (FFM,

p<0.03) and RMR (p<0.05). Feelings of fullness (p<0.02) and satiety (p<0.04) were increased and feelings of hunger (p<0.02) were decreased by CLA. However, CLA did not affect EI. The effect of CLA on FFM, RMR and parameters of appetite were independent of %regain. In conclusion, fat free mass, resting metabolic rate and appetite were favorably affected dose-independently by a 13-week consumption of 1.8 or 3.6 g CLA/d. However, this did not result in a lower energy intake measured at breakfast or in an improved body weight maintenance.

Adult picky eating: is there more to it? J. KAUER, *University of Pennsylvania, Dept. Anthropology, Philadelphia, PA 19104-6398, USA,* P. ROZIN, *University of Pennsylvania, Dept. Psychology, Philadelphia, PA 19104-6196, USA,* M.L. PELCHAT, *Monell Chemical Senses Center, Philadelphia, PA 19104-3308, USA.*

Picky eating (e.g., eating a very small range of foods, not letting foods touch on the plates, food neophobia) is a major topic in children's food selection research. However, there has been no research on the specifics of adult picky eating. Thus, we surveyed 489 representative adults from Philadelphia to examine food selection patterns. This database was used to select extremely picky and non-picky eaters. These subjects underwent chemosensory testing, completed a number of psychological tests, and were interviewed. We found significantly higher scores for the PICKY group for a number of psychological scales, including Food Neophobia (but not General Neophobia), Padua Inventory for Obsessive-Compulsive Disorder, Beck Depression Inventory, and the Disgust Scale. We also found higher ratings by the PICKY of sucrose and quinine intensity. There were no differences in the groups' ratings of PROP intensity. Subjects in the PICKY group reported high levels of social and psychological discomfort due to their eating habits vs. those in the NONPICKY group. Interestingly, although they reported their eating habits caused major social disruption and anxiety, only 47% of PICKY subjects said that they would accept a (hypothetical) simple treatment to allow them to eat from a wide range of foods. Finally, across groups, most people like eating too much to accept a "food pill" in lieu of having to eat, and this was not significantly different between the PICKY and NONPICKY groups.

Beginning a new nutrition conversation with consumers: Creating messages that work. L. KELLY, S.T. BORRA, S. ROWE, S. GOLDBERG, *International Food Information Council, Washington, DC, USA.*

Nutrition communications are key to all health professionals' success in motivating healthy eating and physical activity behavior change. However, sometimes the path of nutrition communications follows a one-way street — messages reach the consumer, but do we know how, or even if, these communications have impact? Does behavior change occur? Advertisers and marketers often use a five-step process to obtain consumer input about a potential product or campaign. It became apparent that marketing models used to sell tangible "products" can also be applied to the food, nutrition, and physical activity "product." The International Food Information Council utilized a marketing tool to develop message concepts on dietary fats and sweet foods and beverages. Through a series of consumer focus groups, creative message development, and qualitative validations, several basic message concepts were developed which resonate with consumers. By utilizing this process, health professionals can maximize communications with clients, and facilitate the maintenance of balanced, healthful lifestyles. Knowing what consumers are thinking and feeling about their food choices, why they make the decisions they do, and how they respond to nutrition messages are essential to successfully communicating and motivating behavior. Subsequently, dietary information can be conveyed in a way that is received in an understandable and actionable manner by consumers. In other words, a dialogue to talk with consumers, rather than at them, should be established.

Stressful experience early in life modulates gene expression of neuropeptide y in the arcuate nucleus of rats in late age. H.J. KIM, D.G. KIM, J.W. JAHNG, *Yonsei University, College of Medicine, Seodaemoon-gu Seoul outside of U.S. 120-752, South Korea*

The hypothalamic-pituitary-adrenal (HPA) axis plays an important role in the regulation of feeding behavior as well as stress responses. In rats, stressful experiences early in life, such as mother-pup separation, result in alteration of HPA axis and basal plasma glucocorticoids in adulthood. Plasma glucocorticoids mediate expression of hypothalamic feeding peptides including NPY. We examined mRNA levels of NPY, known as the most potent orexigenic molecule, in the arcuate nucleus of rats experienced mother-pup separation during the first two weeks of birth. Male pups were culled on postnatal day (PND)1, each litter was subjected to each different conditions, that is, non-disturbed (non-handled), removed from their home cage and dam for 15min (handled), or for 180min (separation) every morning during PND1 through 14, then left with their own dams

until weanling. Body weights were measured weekly, and rats were sacrificed on PND 60, forebrain sections processed for in situ hybridization with NPY cDNA probe. Half of rats from each litter were food-deprived for 48h prior to the histochemical process. Basal expression level of NPY appeared to increase in handled and separation with no statistical significances, however, fasting-induced increase of NPY expression was significantly bigger in handled and smaller in separation group, compared to non-handled group. Body weight gain did not differ in all groups. These results indicate that stressful experiences early in life may not have a significant influence on the basal NPY expression, but could modulate NPY expression responding to stress challenges like food deprivation, and possibly produce disorders in body weight regulation consequently.

Dexamethasone prolongs, RU486 facilitates, the extinction of lithium-induced conditioned taste aversion in rats. J.T. KIM, D.G. KIM, J.W. JAHNG, *Dept. of Pharmacology and Yonsei Brain Research Institute, BK21 Project for Medical Science, Yonsei Univ. College of Medicine, Seoul, 120-752, Korea.*

Lithium chloride is a widely used unconditioned stimulus in conditioned taste aversion (CTA) learning. Intraperitoneal injection of lithium chloride induces ACTH release and activates hypothalamic-pituitary-adrenal (HPA) axis. It has been reported that pharmacologic manipulation of HPA activity modulates lithium-induced CTA. Acute lithium chloride at large dose induces c-Fos expression in the brain regions implicated in CTA learning, such as the hypothalamic paraventricular nucleus (PVN), central nucleus of amygdala (CeA), and nucleus tractus of solitarius (NTS), and it was reported that c-Fos induction in these brain regions is correlated with CTA formation. In this study, we examined the effects of dexamethasone (DEX) pretreatment at conditioning on lithium-induced CTA and brain Fos expression, and the effects of glucocorticoid receptor antagonism using RU486 at conditioning with lithium chloride was also determined. Inhibition of HPA activation by a large dose of DEX prior to lithium chloride significantly attenuated lithium-induced c-Fos expression in the PVN and NTS, but not in the CeA. By DEX pretreatment at conditioning, the acquisition of lithium-induced CTA was not affected but the extinction was prolonged. RU486 prior to lithium produced no effect on the acquisition, but facilitated the extinction. We conclude that HPA suppression at the conditioning may not affect CTA acquisition, and increased plasma glucocorticoids by lithium chloride may affect the neural circuit implicated in aversive memory retention.

The diverse role of specific GLP-1 receptors in the control of food intake and the response to visceral illness. K.P. KINZIG, D.A. D'ALESSIO, R.J. SEELEY, *Dept. of Psychiatry, University of Cincinnati College of Medicine, Cincinnati, OH 45267, USA.*

Intracerebroventricular administration of glucagon-like peptide-1 (7-36) amide (GLP-1) reduces food intake and produces symptoms of visceral illness such as a conditioned taste aversion. The central hypothesis of the present work is that separate populations of GLP-1 receptors mediate the anorexia and taste aversion associated with GLP-1 administration. To test this hypothesis, we first compared the ability of various doses of GLP-1 to induce anorexia or conditioned taste aversion when administered either into the lateral or fourth ventricle. Lateral and fourth ventricular GLP-1 resulted in reduction of food intake at similar doses, while only lateral ventricular GLP-1 resulted in a CTA. Such data indicate that both hypothalamic and caudal brainstem GLP-1 receptors are likely to participate in GLP-1's ability to reduce food intake. We further hypothesized that the site that must mediate GLP-1's ability to induce visceral illness is in the central nucleus of the amygdala (CeA). Administration of 0.2 µg or 1.0 µg doses into the CeA result in a strong conditioned taste aversion but no reduction in food intake. Taken together, these data indicate that separate GLP-1 receptor populations mediate the multiple responses to GLP-1. This makes GLP-1 a flexible system that can be used under differing circumstances to alter the ingestion of nutrients and/or produce other visceral illness responses depending on the ascending pathways of the GLP-1 system that are recruited.

Combined Effects of Suprathreshold Gastric Distention and CCK-8 on Food Intake in Humans - Preliminary Report. H.R. KISSILEFF, M. TORRES, A. GELIEBTER, F.X. PI-SUNYER, *New York Obesity Research Center, St. Luke's-Roosevelt Hospital Center, Columbia University, New York, NY 10025, USA.*

To determine whether a combination of suprathreshold doses of CCK and gastric distention would lead to a greater reduction in food intake, than near threshold doses, 5 men and 7 women ate yogurt shake (1.04 kcal/g) test meals under four conditions: infusion of CCK-8 (168 ng/min for 30 min before the meal) or saline, crossed with distention induced by a balloon in the stomach that was filled with 450 ml water or not filled. The results were compared with a previous group of 16 subjects who received 112 ng/min of CCK for 21 min and 300 g

distention. The combined effect of 168 ng/min CCK and 450 ml distention (383 g) resulted in a significant ($p < .0001$) 404.7 g ± 77 SED reduction compared with saline and no distention(785 g). This difference was 204 g ± 82.94 SE more ($p = .021$) than the corresponding reduction (200g ± 43 SED) in the previously studied group. The three components of this difference were attritutable to CCK without distention (107 g), distention without CCK (52 g) and interaction (44 g). Therefore, the combined effect at the higher CCK and distention dose is more attributable to the direct effects of CCK than to the CCK x distention interaction. (NIDDK53089, RODDK26687).

Salt preference in patients with CAH-21-OH deficiency (congenital adrenal hyperplasia). A. KOCHLI, Y. RAKOVER[1], M. LESHEM, *Dept. of Psychology, 31905 Haifa University, [1]Pediatric Endocrine Unit, Ha'Emek Medical Center, Afula, Israel.*

Little is known about the determinants of salt intake in humans. Studies have failed to confirm the common belief that increased salt intake is due to availability and dietary habits established in infancy. In contrast, research in animals has shown that salt intake is determined by physiological and genetic factors. In humans, the only reports of physiologically-related salt appetite have been sporadic and anecdotal, in cases of Addison's disease. We studied salt appetite in CAH patients with various mutations of the CAH-21-OH gene, comparing their salt appetite to that of their relatives. Here we present some of our preliminary findings. We show that adrenal hyperplasia in its most severe form (salt wasting) increases a number of indices of salt preference, providing empirical support for clinical observations. Our findings do not support previous reports of altered taste sensitivity reported for Addison's patients, but we find increased hedonic evaluation of high concentrations of salt in salt-wasting patients. These findings suggest that physiology contributes to salt appetite in humans.

Alteration of the microstructure of feeding behavior during the first meal of a threonine-imbalanced diet. T.J. KOEHNLE, A. STEPHENS, D.W. GIETZEN, *School of Veterinary Medicine, University of California at Davis, Davis, CA 95616, USA.*

Previous work demonstrated that rats fed a threonine-imbalanced diet (ThrImb) significantly reduced their rate of eating compared to rats fed an amino acid corrected diet (Cor) within the first 8-12min of their first meal. For this investigation, 13 male Sprague-Dawley rats were trained for 15d to consume their daily food requirement of a basal diet (Bas) in 6h. Rats fed ThrImb (n=7) quickly recognized the imbalance. Behavioral rejection of this diet was manifested in four ways: 1) significant reduction in duration of the first meal relative to meal duration on Bas (from 42±7.0min to 18±2.6min, $p=0.005$); 2) significant reduction of meal size compared to intake on Bas (from 7.35±1.00g to 3.64±0.49g, $p=0.004$); 3) significantly decreased eating bout durations within the meal ($X2(4)=41.49$, $p<0.001$) compared to rats fed Cor (n=6), characterized by more short bouts during the first half of the meal ($X2(3)=21.89$, $p<0.001$);and 4) significantly higher frequency of short pauses in the first half of the meal compared to rats fed Cor ($X2(4)=18.30$, $p<0.005$), and significantly higher frequency of long pauses during the second half of the meal ($X2(4)=15.32$, $p<0.005$). Duration of the first intermeal interval compared to Bas was unchanged in both Cor and ThrImb groups, and was not correlated with either total intake or duration of the first meal. These data suggest that rats reject imbalanced diets by alteration of pause and bout structure, in addition to previously reported changes in rate of eating. This work was supported by USDA grant 2000-01049 and NIH grant NS 33347.

The effects of enterostatin intake on food intake and energy expenditure. E.M.R. KOVACS, M.P.G.M. LEJEUNE, M.S. WESTERTERP-PLANTENGA, *Dept. of Human Biology, Maastricht University, Maastricht, The Netherlands.*

Enterostatin has been found to inhibit food intake and selectively inhibit fat intake in rats. Both peripheral and central mechanisms have been proposed. It also has been suggested that enterostatin may increase thermogenesis. This study investigated the effects of oral enterostatin administration on food intake, energy expenditure and body weight in subjects with a preference for a high-fat diet. In a double-blind, placebo-controlled, randomized and crossover design, nine female and three male healthy subjects (mean±SD; age, 34±11 y; BMI, 24.5±2.5 kg/m2) with a preference for a high-fat diet ingested enterostatin (ENT) or placebo (PLA) 3x15 mg/day while consuming an ad libitum 4-day high-fat diet. Eight subjects ended each intervention with a 36-h stay in the respiration chamber, continuing the diet and treatment. Body weight loss was significant (mean±SE; ENT, 0.8±0.3 kg, $p<0.05$; PLA, 1.3±0.3 kg; $p<0.001$), but not different between treatments. There was no difference between treatments in total energy intake (ENT, 37.1±2.6 MJ; PLA, 35.9±3.2 MJ), macronutrient composition, hunger, satiety and hedonic scores during the 4-day high-fat diet. 24-h energy expenditure (ENT, 9.6±0.4 MJ; PLA, 9.5±0.4 MJ), sleeping and resting metabolic rate, diet-induced

thermogenesis, activity-induced energy expenditure and 24-h respiratory quotient (ENT, 0.77±0.01; PLA, 0.77±0.01) were similar for both treatments. We conclude that oral enterostatin administration did not affect food intake, energy expenditure or body weight in subjects with a preference for a high-fat diet.

Increasing the portion size of a packaged snack increases energy intake. T.V.E. KRAL, L.S. ROE, J.S. MEENGS, D.E. WALL, B.J. ROLLS, *Nutrition Dept., The Pennsylvania State University, University Park, PA 16802, USA.*

Portion sizes of packaged snack foods have increased recently, but the effect of such increases on energy intake has not been systematically investigated. In a controlled study, we examined the effect of the package size of a snack food on intake, both during the snack and at the following meal. On five separate days, 30 female and 24 male subjects ate an afternoon snack and dinner in the laboratory. At each snack, subjects were served one of five package sizes of potato chips: 28 g, 42 g, 85 g, 128 g, or 170 g. The packages were unlabelled, and the order of presentation of the package sizes was randomized across subjects. Results showed that the package size of potato chips had a significant effect on snack intake for both male and female subjects ($p < 0.0001$). Most subjects did not consume all of the potato chips in the 85 g (3 oz.) package, yet when they were served the 170 g (6 oz.) package, females ate 18% more and males ate 35% more than when served the 85 g package. Despite differences in snack intake, female subjects had no significant differences in energy intake at dinner. Males showed a decrease in intake only after being served the largest snack package. Thus, increasing the size of a packaged snack led to increased energy intake in the short-term. The recent increases in portion size of commercial snack foods may be contributing to increased energy intakes. (Supported by DK59583).

Estrogen attenuation of stimulated water intake is specific to angiotensin II. E.G. KRAUSE, K.S. CURTIS, L.M. DAVIS, R.J. CONTRERAS, *Florida State University, Program in Neuroscience, Dept. of Psychology, Tallahassee, FL 32306-1270, USA.*

Previous experiments from our laboratory indicate that estrogen (EB) decreased water intake following water deprivation. To determine whether EB effects on stimulated water intake are specific to osmotic or angiotensin II (ANGII) mediated drinking we examined water intake after injection of hypertonic saline or isoproterenol in adult Sprague Dawley female rats. Rats were ovariectomized (OVX) and allowed one week to recover. OVX rats were treated with EB (.10mg/.1ml oil) or vehicle (.1ml oil) for two consecutive days. 48h after the second EB treatment OVX rats were injected subcutaneously with hypertonic saline (1ml of 2M NaCl) or isoproterenol (30mg/kg in .15M saline). Following the injection rats were given access to water in graduated tubes and intake was measured every 15min for 2h. To evaluate if drinking stimuli are comparable in EB or oil treated animals, we examined plasma sodium (pNa) concentration or plasma renin activity (PRA) after subcutaneous injection of hypertonic saline or isoproterenol in female rats. The same procedure that was used to assess water intake was used to determine pNa and PRA, except animals were not given access to water. 30min after the injections of hypertonic saline or isoproterenol, blood samples were taken to determine pNa concentration or PRA. Estrogen significantly attenuated water intake following injection of isoproterenol, but not hypertonic saline. There was no difference in pNa concentration of animals treated with EB or oil. Studies examining PRA are ongoing. The results suggest that estrogen specifically modulates water intake elicited by peripheral increases in ANGII. Supported by NIDCD(DCD04785-01).

Systemic MK801 increases intraoral intake of sucrose. B.S. KWON, S.H. CHOI, J.W. JAHNG, T.A. HOUPT, *Dept. Biological Science, The Florida State University, Tallahassee, FL 32306-1270, USA, and Dept. Pharmacology, BK21 Project, Yonsei University College of Medicine, Seoul, Korea.*

When administered prior to food access, the non-competitive NMDA receptor antagonist MK801 increases consumption of rodent chow or 15% sucrose in food-deprived rats, or palatable cookies in non-deprived rats (Burns, Ritter and others), or the first spontaneous meal of the dark period (Jahng and Houpt 2001). Because MK801 increases intake when the rat initiates feeding (i.e. after deprivation or at lights-off), it is hypothesized that MK801 increases feeding not by increasing meal initiation, but by delaying meal termination. Here we employed intraoral catheters to separate appetitive behaviors from consummatory behaviors. Twelve female rats were implanted with intraoral catheters. The rats were habituated to intraoral infusions of sucrose until stable intakes were achieved during 20 ml/min infusions of 15% sucrose. Intake was measured by weighing rats immediately before and after infusion. Non-deprived rats were injected with 0, 25, 50, and 100 ug/kg MK801 in 1 ml/kg 0.15M NaCl. Fifteen minutes later, rats received a 20 ml/20 min infusion of 15% sucrose. Rats received a second injection and infusion 24 h later, with dose counterbalanced across groups. We found that MK801 (100ug/kg) significantly increased intraoral intake of 15% sucrose (17.3 +/- 0.5 g vs. 13.3 +/- 0.9 g, $p < 0.01$).

Because intraoral meals are imposed rather than initiated by the rats, this suggests that MK801 delays termination rather than enhancing initiation. Because intraoral infusion makes ingestion independent of other somatic behaviors, we conclude that MK801 does not delay meal termination by interfering with competing non-ingestive behaviors. Supported by NIDCD03198.

Central glucagon-like peptide-1 (GLP-1) administration supports conditioned taste aversion learning in wild-type mice, but not in mice with a targeted disruption of the GLP-1 receptor (GLP-1R -/-). J.L. LACHEY, D.A. D'ALESSIO, D.J. DRUCKER, R.J. SEELEY, *Dept. of Psychiatry, University of Cincinnati, Cincinnati, OH 45267-0559, USA.*

Many responses characterize visceral illness including anorexia and conditioned taste aversion (CTA) learning. While LiCl, commonly used to induce visceral illness, and central GLP-1 elicit these responses, they are attenuated by a GLP-1 receptor antagonist suggesting that the central GLP system mediates visceral illness. Conversely, LiCl induces equivalent anorexia and CTA formation in wild-type and GLP-1R -/- mice. One explanation for this discrepancy is that, unlike rats, mice do not demonstrate visceral illness responses to GLP-1. To address this hypothesis, we tested the ability of central GLP-1 administration to support CTA learning in the mouse. Pairing a central 5 µg GLP-1 injection with a novel flavor significantly reduced intake of that flavor in a future exposure (control: 2.28±0.1 ml; GLP-1: 1.18±0.14 ml; $p<0.001$) indicating that GLP-1 induces visceral illness in mice as well as rats. The discrepancy between the antagonist and knockout data could be due to GLP-1 acting at a receptor other than the described GLP-1 receptor to produce visceral illness effects. To address this, we tested the ability of GLP-1 to produce a CTA in GLP-1R -/- mice. Consistent with GLP-1R mediating the visceral illness effects of GLP-1, central GLP-1 (5 µg) administration does not support CTA learning in GLP-1R-/- mice (control: 2.29±0.25 ml; GLP-1: 1.83±0.15 ml; $p=0.15$). Thus, the discrepancy between the pharmacological and genetic data on the role of GLP-1 in mediating the effects of visceral illness is neither a species difference in the response to GLP-1 nor recruitment of an unidentified GLP-1 receptor.

Pair-feeding normalizes body weight in bombesin receptor subtype 3 deficient mice. E.E. LADENHEIM, L.E. BARON, L.L. HAMPTON, J.F. BATTEY, T.H. MORAN, *Dept. of Psychiatry & Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.*

Mice lacking the bombesin receptor subtype 3 (BRS-3 KO) develop hyperphagia and obesity beginning at approximately 12 weeks of age. To determine whether their obesity is a direct result of increased food intake or due to a defect in energy regulation, we assessed the effect of caloric restriction on body weight gain in BRS-3 KO mice. Mice were divided into three dietary groups consisting of: 1)ad lib fed wild-type (WT) control mice (n=6) 2) ad lib fed BRS-3 KO mice (n=6) and 3) BRS-3 KO mice (n=5) that were pair-fed to the average daily food intake of the ad lib fed WT control group. At 12 weeks of age, food intake was significantly greater in BRS-3 KO mice compared to WT mice. By week 21, the average daily food intake for ad lib fed BRS-3 KO mice was 4.0 +/- 0.12 g and 3.5 +/- 0.09 g for ad lib fed WT mice. Although BRS-3 KO ad lib fed mice were 27% heavier than WT mice, the body weights of pair-fed BRS-3 KO mice did not differ significantly from WT control mice. These results suggest that the primary cause of obesity in BRS-3 KO mice is increased food consumption and not a dysregulation of energy balance. Supported by NIH grant DK46448.

Hepatic vagotomy completely attenuates the changes in food intake and hypothalamic peptide expression in streptozotocin diabetic rats fed a high-fat diet or given the choice of lard. S.E. LA FLEUR, S. MANALO, M.F. DALLMAN, *Dept. of Physiology, UCSF, Box 0444, 513 Parnassus Avenue, San Francisco, CA 94143, USA.*

Streptozotocin-diabetic rats are hyperphagic and show low hypothalamic CRFmRNA and high NPYmRNA when fed a high-carbohydrate (HC) diet. Switching to a high-fat (HF) diet restores food intake and normalizes mRNA signals. How the brain senses these changes in diet is not known. We tested whether the vagal pathway mediated the signal of the HF-diet to the brain. We hepatic-vagotomized or sham-vagotomized rats. After recovery, they were made diabetic with streptozotocin and introduced to a HC-diet. After 6d, half of the rats were switched from the HC-diet to a HF-diet. 5d after diet change, rats were decapitated. In a second experiment, rats were also hepatic-vagotomized or received sham-surgery. Following recovery, rats received either streptozotocin or a vehicle injection (resulting in four groups of rats: Vag-Diab, Vag-Veh, Sham-Diab, Sham-Veh). All groups were given a HC-diet. After 6d, half of each rat group received the HC-diet with a cup of lard, whereas the other half had access only to the HC-diet. 3d later, all rats were decapitated. During the experiments, caloric intake and body weight were recorded daily. Plasma and brains were collected for hormone analysis and immunocytochemistry at the conclusion of both experiments. Switching diabetic rats from HC-diet

to HF-diet or to HC-diet with lard resulted in an inhibition of food intake to non-diabetic levels. This was accompanied by a normalization of 'food intake'-related peptides. Strikingly, hepatic-vagotomy attenuated these fat-induced changes completely. Since non-diabetic rats were not affected by eating fat, this suggests that autonomic feedback is affected in diabetes. Supported by 'Dutch Diabetes Research Foundation' & DK28172.

Toward and understanding of the neurobiolgical contribution to contribution to anorexia nervosa. B. LASK, *Dept. of Psychiatry, St George's Hospital Medical School, Cranmer Terrace, London SW17 0RE, UK.*

Over the last few years there have been an increasing number of neuroimaging studies in patients with anorexia nervosa (AN). Structural imaging (computerised tomography, CT) and magnetic resonance imaging (MRI) have shown changes such as sulcal widening and ventricular enlargement, which are reversible with weight gain in the majority of cases. Functional imaging studies using positron emission tomography (PET) in adults with AN have suggested that there may be a focal lesion, with findings such as low relative values of glucose metabolism in the parietal cortex compared with healthy controls and increased relative glucose metabolism in the inferior cortex and caudate. Regional cerebral blood flow (rCBF) studies using single photon emission computerised tomography (SPECT) in adult patients with AN have been inconclusive. In children and adolescents with AN a number of studies have shown reduced cerebral blood flow within the temporal lobe and areas adjacent to it. These findings all indicate the possibility of some form of circuit dysfunction, possibly due to limbic system imbalance. The findings will be discussed in detail, the limbic system hypothesis presented, and a paradigm for further research will be discussed.

Proteomic analysis of the rat hypothalamus experienced mother-pup separation early in life. J.Y. LEE, S. LEE, D.G. KIM, J.W. JAHNG, *Dept. of Pharmacology and Yonsei Brain Research Institute, BK21 project for Medical Sciences, Yonsei University College of Medicine, Seoul, 120-752, Korea.*

The HPA axis plays an important role in the regulation of feeding behavior as well as stress response. It was reported that stressful experience early in life such as mother-pup separation results in the alteration of HPA axis and basal level of plasma glucocorticoid in adulthood. Alteration of HPA axis could affect the expression of hypothalamic feeding peptides, such as NPY expression is regulated by plasma corticosterone, may cause eating disorders as a consequence. In this study, we examined the hypothalamic protein patterns of rats experienced mother-pup separation early in life by proteomic analysis technique. Every morning between 9:00 AM and 12:00 PM, pups were subjected to three different conditions [1) non-handled; non-disturbed, 2) handled; removed from their home cage and dam for 15 min daily, 3) separation; remove from their home cage and dam for 180 min daily] from PND 1 till PND 14, then left in their own cage with the dam until weaning. On PND 60, rats were rapidly decapitated and the hypothalamic tissues were collected and stored at –80°C until used. Tissues were homogenized in Reagent 3 buffer and centrifuged. Supernatants were isoelectrofocused using PROTEAN IEF CELL (Bio-Rad) with IPG strips (pH 4-7), then electrophoresed on 12% of SDS-PAGE. The SDS gels were Coomassie stained and overall 500 of protein spots revealed on each gel. Twenty eight protein spots appeared to be down-regulated, 15 spots up-regulated, in handled and separation groups, compared to non-handled group. These protein spots were analysed by MALDI-TOF peptide analysis system.

The hypophagic action of 5-HT2C agonists is attenuated in mice lacking functional 5-HT1B receptors. M.D. LEE[1], G.A. KENNETT[2], C.T. DOURISH[2], P.G. CLIFTON, [1]*Expt. Psychology, Univ. Sussex, Brighton, BN1 9QG, UK.* [2]*Vernalis Res, Wokingham, RG41 5UA, UK.*

Targeted deletion of the 5-HT1B receptor in mice leads to hyperphagia, increased body weight, and a blunted response to d-fenfluramine-induced hypophagia (Olivier et al. 2002; Clifton et al 2001). We have also shown that the anorectic effect of the selective 5-HT1B agonist, CP-94,253, is absent in these mice (Lee et al. 2001). Here we characterise the effect of the 5-HT2C/1B receptor agonist mCPP and the selective 5-HT2C agonist Ro-60,0175, in mice consuming a test meal of palatable wet mash. mCPP (0,1,3,5.6 mg/kg IP) or Ro-60,0175 (0,3,5.6,10 mg/kg IP) were given to separate groups of mutant and age-matched wild-type mice (N=12/genotype) 30 min before food presentation. mCPP reduced mash intake in wild-type mice in a dose-dependent manner (28%,38% and 67% at each dose compared to vehicle; $P<0.001$). However, the hypophagic effect of mCPP was completely absent in knockout mice at the lower doses (1,3 mg/kg), and blunted at 5.6 mg/kg (40% decrease). Similarly, food intake in wild-type mice was decreased by Ro-60,0175-administration at doses of 5.6 and 10 mg/kg, but only at 10 mg/kg in knockout mice. Analyses of time-sampled observations indicated that both mCPP and Ro-60,0175 promote satiety without disrupting the organisation of feeding-related

behaviour. These data suggest that loss of 5-HT1B receptors early in development may lead to changes in the functional sensitivity of 5-HT2C receptors. The impact of these findings on transgenic studies of serotonin function will be discussed. Supported by BBSRC-LINK.

Effect of dietary restraint during and following pegylated recombinant leptin treatment (PEG-OB) of overweight men. M.P.G.M. LEJEUNE, C.J. HUKSHORN, W.H.M. SARIS, M.S. WESTERTERP-PLANTENGA, *Dept. of Human Biology, Maastricht University, PO Box 616, 6200 MD Maastricht, The Netherlands.*

Changes in attitude towards eating measured with the Three Factor Eating Questionnaire (TFEQ) following a weight reduction program have been observed in that these support weight maintenance. The question remains whether pharmacological treatment, i.e. pegylated recombinant leptin (PEG-OB protein) treatment replaces or supports cognitive dietary restraint (F1 of TFEQ) during treatment. To examine the effect of F1 during and following PEG-OB protein treatment, we performed a randomized double blind placebo controlled trial in 24 moderately overweight men (BMI: 28.8±0.3 kg/m2; age: 34.8±0.9 yrs). PEG-OB protein (80 mg) or placebo was administered subcutaneously weekly for 6 weeks, combined with a 2.1 MJ/d energy restriction program. F1 was determined by the TFEQ before and after the treatment, and after 8 weeks follow-up. During treatment F1 increased (from 5±1.0 to 12±1.2) similarly in the PEG-OB and the placebo group. Body weight (BW) loss was 14.6±0.8 with PEG-OB and 11.8±0.9 with placebo ($p<0.03$). During 8 weeks follow-up, body weight increase was larger in the PEG-OB group compared to placebo ($p<0.05$), and BW regain was faster (0.48 %/d vs. 0.27 %/d). BW regain was inversely correlated with the increase in cognitive dietary restraint during treatment (PEG-OB group: $r2=0.49$; $p<0.02$; placebo group: $r2=0.60$; $p<0.01$). Although treatment with PEG-OB protein led to a greater BW loss relative to placebo, weight maintenance thereafter was mainly supported by F1. We conclude that pharmacological treatment may limit the change in lifestyle necessary for weight maintenance after weight loss.

Reversal of inflammation-induced anorexia by ICV injection of SHU9119. T.A. LENNIE, *College of Nursing, The Ohio State University, Columbus, OH 43210-1289, USA.*

Previous research demonstrated that reductions in body weight prior to induction of acute inflammation decreases circulating leptin levels and reverses inflammation-induced anorexia. Because leptin has been shown to lower food intake by increasing hypothalamic levels of a-melanocyte stimulating hormone (a-MSH), we hypothesized that a-MSH may be involved in inflammation-induced anorexia. To test this hypothesis, four groups of ad-libitum fed rats and four groups of weight-reduced (-12%) rats with cannulas implanted into the 3rd ventricle were studied. Two groups of normal-weight (NWC) and two groups of reduced-weight (RWC) rats served as controls; while the remaining two normal-weight (NWI) and reduced-weight (RWI) groups received subcutaneous turpentine injections. Six hours after induction of acute inflammation, rats received ICV injections of either 0.25 nmol of SHU9119 or 2 ul of normal saline. All rats were given ad libitum access to food at the onset of the dark cycle. Food intake and body weight were measured for the next week. The twenty-four hour food intake for Day 1 post-inflammation was: CON/Saline: 23 g.; CON/SHU 28 g; NWI/saline: 11g; NWI/SHU: 24 g; RWC/Saline: 28 g; RWC/SHU 30 g; RWI/Saline: 24 g; RWI/SHU: 28 g.; (n = 4/group). These preliminary results show that ICV injection of SHU9119, an a-MSH antagonist, reverses inflammation-induced anorexia resulting in food intakes that resemble intakes of control and weight reduced rats. Additional research is underway to further clarify the role of a-MSH and to identify other peptides that may be involved in mediating inflammation-induced anorexia. (Supported by NINR NR04783)

Hepatic portal vein infusion of caprylic acid decreases food intake by reducing the size and number of meals in male rats. M. LEONHARDT, U.L. JAMBOR DE SOUSA, W. LANGHANS, *Institute of Animal Sciences, Swiss Federal Institute of Technology, 8603 Schwerzenbach, Switzerland*.

Hepatic fatty acid oxidation is implicated in the control of food intake. We therefore tested the effects of hepatic portal vein infusions of the medium-chain fatty acid caprylic acid (CA) on feeding and plasma metabolites in male rats. In Experiment 1, CA or equimolar saline (control) was infused (1.3ml/h, total dose: 2.7mmol) for 6 h starting at one hour before lights off. Rats were food deprived for two hours prior to lights off, when food cups were reopened. At infusion end a jugular vein blood sample was taken for analyses of plasma β-hydroxybutyrate, free fatty acids, glucose and insulin. CA reduced 12h cumulative food intake (control: 19.3±0.9g, caprylic acid: 14.7±1.3g, $P< 0.05$), but had no clear effect on meal patterns or the examined blood parameters. In Experiment 2, rats were fasted for 18h. At lights off, food cups were opened and control or CA

infusion (2.3ml/h x 1.5h, total dose: 1.19mmol) began. CA again reduced 12 h cumulative food intake (control: 26.6±1.6g, caprylic acid: 20.3±2.0g, P< 0.01) and this effect was due to a reduction in the size of the first two meals (Meal 1: 7.0±0.8g vs 3.6±0.5g, P<0.001 and Meal 2: 3.6±0.4g vs 2.2±0.4g, P<0.05) and a decreased number of meals during the dark phase (7.5±0.5 vs 6.3±0.5, P<0.01). These results show that CA infusion into the hepatic portal vein inhibits feeding by reducing the size and number of meals. It remains to be determined whether these effects are due to an enhanced hepatic oxidation of CA.

Stress and the obese rat: on being fat and happy. B.E. LEVIN, S. BROWN, C. MICHEL, *VA Medical Center, East Orange, NJ 07018, USA*

There is a conflicting literature on the relationship between chronic stress and obesity. We have used a rat model of diet-induced obesity (DIO) or diet-resistance (DR) to assess the metabolic and homeostatic consequences of a variety of chronic stressors. DR rats were highly responsive to low level, daily, unpredictable stress and showed no desensitization. When fed a moderate fat diet (31%) or highly palatable liquid diet (Ensure), they lost weight and had significant elevations of basal morning plasma corticosterone as compared to their unstressed DR controls. Paradoxically, they had lower levels of 24h urine norepinephrine excretion suggesting reduced sympathetic activity. Terminally, chronically stressed DR rats had elevated paraventricular nucleus corticotropin-releasing hormone mRNA expression. On the other hand, DIO rats were relatively unresponsive to the same level of chronic stress. They lost no weight and had no change in their basal morning plasma corticosterone levels or 24h urine norepinephrine levels. Their terminal levels of paraventricular corticotropin-releasing hormone mRNA expression were comparable to unstressed DIO controls. Thus DIO rats are hyporesponsive to chronic stress compared with DR rats. This is in keeping with several other known differences in hypothalamo-pituitary and autonomic function in this rat model of polygenic obesity.

We eat what we're served: Effect of portion size on food intake. D.A. LEVITSKY, T. YUN. *Division of Nutritional Sciences and the Dept. of Psychology, Cornell University, Ithaca, NY 14853, USA.*

The present study examined of the effects of portion size on the amount of food young adults consume. Thirteen students were given lunch on Monday, Wednesday and Friday for two consecutive weeks. For the first session, soup, pasta, bread, and ice cream were available from a buffet table. After subjects took their food, it was weighed. After they finished eating, what was left on their plates was also weighed. For the second week, the subjects were divided into three groups with one group being served a portion of each food that was 100% of the amount they consumed during the first session. The second group received 125%, and the third was served 150%. On each succeeding session the groups rotated in a counterbalanced order through the different portion sizes. The data demonstrated quite clearly that as portion size increased, so did the subject's consumption. What was remarkable was that the effect was statistically significant for almost every food served. These results, along with other studies from the literature, demonstrate the sensitivity of human eating behavior to portion size and suggests that the increase in size of portions offered in restaurants and fast food establishments over the past years may be a major reason for the increase in overweight and obesity evident in our population today.

Melanin-concentrating hormone receptor antagonists decrease food intake in rodents. D.R. LEWIS, M.A. JOPPA , S. MARKISON, K.R. GOGAS, D.A. SCHWARZ, F. ZHU, R.A. MAKI, A.C. FOSTER, *Neurocrine Biosciences, Inc., Dept. of Neuroscience, San Diego, CA 92121*, *USA.*

Evidence suggests that melanin-concentrating hormone (MCH) is one of several hypothalamic peptides involved in the regulation of feeding behavior and energy balance. MCH administration increases food intake and antagonism of this system may prove to effectively inhibit ingestion. We have begun to investigate the effects of selective MCH receptor (SLC-1) antagonists on feeding using several paradigms. Two antagonists, NBI-1A and NBI-1B (0-30 mg/kg, i.p.), dose-dependently reduced feeding during the first hour of a 6-hour observation in food-deprived Wistar rats (n=8/group; P<0.005) and in deprived CD-1 mice (n=10/group; P<0.0008). NBI-1B given orally (3-30 mg/kg) to rats was equally effective (P<0.05). In these experiments, motor activity was simultaneously measured and reduced (Ps<0.009) by i.p. administration but not by oral delivery. Furthermore, in an open field test in mice, only the highest antagonist dose (30 mg/kg, i.p.) suppressed activity in the 10-min test. The lower doses that did suppress feeding (0.3 & 3 mg/kg) did not alter locomotion. Taken together, it appears that there is no clear association between the effects of MCH antagonists on feeding and the effects on locomotion. In a third set of experiments, we examined the ability of NBI-1A (i.p.) to antagonize elevated feeding by MCH (intracerebral ventricle) in satiated rats (n=7-8/group). MCH receptor antagonism attenuated MCH-induced feeding (P<0.001) and also suppressed feeding in sated animals. Our findings support the

conclusion that MCH antagonists reduce feeding in multiple feeding paradigms and species, and suggest that MCH antagonists may be useful therapeutic tools in the treatment of obesity.

Toward an understanding of differences in eating regulation between restrained dieters and restrained nondieters. M.R. LOWE, C.A. TIMKO, *MCP Hahnemann University, Philadelphia, PA 19102-1192, USA.*

Restrained eaters who are and are not dieting to lose weight have shown opposite eating regulation patterns in past research. The nature of these differences was studied by comparing these two groups, plus a reference group of unrestrained eaters, on the Cognitive Restraint (CR) scale and the Restraint Scale (RS). All participants were in the normal weight range. Restraint theory and the Three Factor Model of Dieting converged in predicting that Restrained Dieters (RDs) would have higher and more homogeneous CR scores than Restrained Nondieters (RNDs). The two models diverged in their predictions for these groups on the RS. Results were most consistent with the Three Factor Model of Dieting. RDs, relative to RNDs, obtained higher and more homogeneous scores on the CR, and higher and more heterogeneous scores on the RS. These results suggested that RDs might also have a greater weight cycling history than RNDs. A post hoc analysis of a standard measure of weight cycling confirmed this. These findings indicate that 1) the counterregulatory eating of restrained eaters shown in past studies cannot be due to a history of unsuccessful dieting; 2) current dieting status reflects both a state of attempted dietary restriction and a trait of frequent weight cycling in the past; and 3) individuals at greatest risk for overeating are those with an extensive history of dieting who are not currently dieting to lose weight.

Natriorexic behavior induces dopamine release in the nucleus accumbens. L.R. LUCAS, A. HAJNALI[1], C.A. GRILLO, Z. CELEN, B.S. McEWEN, *Lab. of Neuroendocrinology, The Rockefeller University, New York, NY 10021 and [1]Dept. of Behavioral Science, Pennstate University, Hershey, PA 17033, USA.*

Rapid sodium depletion and salt appetite occurs in rats that are administered the diuretic furosemide (FURO). Previously, we have shown that several molecular markers in the mesolimbic dopamine (DA) system are activated in rats that are treated with FURO and allowed access to a salty solution (FURO+salt) compared with those allowed access only to water(FUROnosalt). The purpose of the present study was to examine whether accumbal DA release is correlated with salt intake behavior in FURO+salt vs. FUROnosalt salt-appetitive rats. Rats were implanted with bilateral guide catheters for microdialysis in the caudomedial nucleus accumbens. After 1 week recovery, rats were transferred to microdialysis cages and microdialysis probes were implanted to sample baseline dopamine levels. After baseline measures were established, rats were administered FURO (2 s.c. injections of 5 mg/rat, plus Teklad sodium deficient chow) and given access either to 2% NaCl or tap water for 2 h on the following day. In agreement with out hypothesis, FURO+salt rats increased DA release after 40 min compared to baseline. Furthermore, FUROnosalt rats decreased DA release after 20 min. Both groups returned to baseline at the end of the 2 h monitoring period. The present results add to a growing body of evidence that suggests that the dopaminergic system is directly involved in the execution of motivated behaviors including those associated with the maintenance of fluid and electrolyte balance. Supported by MH43787 (LRL,BMc) and DC04751(AH).

Dose-response analysis of furosemide induced sodium appetite. R.F. LUNDY Jr., M.E. BLAIR, R. NORGREN, *Dept. of Behavioral Science, College of Medicine, The Pennsylvania State University, Hershey, PA 17033-2390, USA.*

Sodium appetite is often produced experimentally by using the diuretic furosemide (Furo) to induce a rapid loss of urinary sodium. The standard dose of Furo is 10 to 14 mg per rat. The present study compared the effects of five different furosemide doses (0.5, 1, 2, 6, and 10 mg) on 0.51M NaCl intake, water intake, Na+-free chow intake, urine volume, electrolyte balance, and weight gain in rats. Six days of baseline measurements were followed by an injection day and a test day. This sequence was repeated 3 more times, 2 with the same dose of Furo, the last with saline. The negative Na+ balance produced by Furo injection was dose dependent but did not change across repeated depletions with 10mg = 6mg > 2mg >1mg = 0.5 mg. The NaCl intake, on the other hand, varied both as a function of dose and trial. In trial 1, all Furo doses produced equivalent intake. Following the second and third depletion, however, the 6 and 10 mg dose increased salt intake compared with the first trial, while that following the lower doses remained unchanged. More importantly, on all trials both food intake and weight dropped significantly following the 2 higher doses of Furo, but not for the 3 lower ones. Given this substantial side effect, the preferred dose of Furo for inducing a salt appetite should not exceed 2.0 mg per rat. Supported by DC 00240, MH 43787, DC 00369, and a Penn State Life Sciences Consortium Award.

Amylin activates hindbrain neurons in areas expressing glucagon-like peptide. T.A. LUTZ[1], A. BLOCH-THOMSEN[2], M. TANG-CHRISTENSEN[2], A. MOLLET[1], D. ZÜND[1], T. RIEDIGER[1], [1]*Institute of Veterinary Physiology, University of Zurich, 8057 Zurich, Switzerland;* [2]*Laboratory of Obesity Research, CCBR, 2750 Ballerup, Denmark.*

Amylin is a satiating hormone acting via area postrema (AP) neurons. Peripheral amylin's anorectic effect is ablated in AP-lesioned (AP-X) rats, and amylin specifically activates AP neurons. We now wanted to further delineate the CNS mechanisms underlying amylin's anorectic action. Anorectic doses of amylin (5-20 micro-g/kg IP) led to a strong expression of c-Fos protein in the AP, nucleus of the solitary tract (NTS), lateral parabrachial nucleus (lPBN) and amygdala (AMG). The effects in the NTS, lPBN and AMG were blocked in AP-X rats. Therefore, the NTS which is an important afferent and efferent relay station connecting the hindbrain with forebrain structures seems to be neuronally activated subsequent to amylin-induced excitation of AP neurons. Interestingly, c-Fos induction in the NTS was seen in areas of the location of glucagon-like peptide-1 (GLP-1) neurons. The latter neurons are believed to form part of an afferent pathway from the gastrointestinal tract to the brain. Further, in vitro studies showed co-activation of AP neurons by amylin and GLP-1. These effects were blocked by the pertinent antagonists (AC187, exendin9-39). This indicates that there may be a link between amylin's effects in the hindbrain and the GLP-1 system. Although GLP-1 has been suggested to be involved in the development of conditioned taste aversion (CTA), it is likely that locally released GLP-1 acts as a hindbrain neurotransmitter to specifically reduce feeding via an activation of amylin-sensitive AP neurons because even high anorectic doses of amylin (20 micro-g/kg) did not induce CTA in a two-bottle preference test.

Amylin activates a dopaminergic pathway in the area postrema. T.A. LUTZ[1], T. RIEDIGER[1], D. ZÜND[1], P. WOOKEY[2], [1]*Institute of Veterinary Physiology, University of Zurich, 8057 Zurich, Switzerland;* [2]*Dept. of Medicine, A&RMC, West Heidelberg, VIC 3081, Australia.*

Pancreatic amylin is considered an important satiating hormone. Peripheral amylin acts via the area postrema (AP) of the hindbrain, as shown by feeding, immunohistochemical (detection of c-Fos) and electrophysiological studies. Within the AP, cGMP is the second messenger responsible for amylin's excitatory effect on amylin-sensitive neurons. A direct action of amylin on AP neurons is supported by our present findings that amylin-sensitive neurons (characterized by cGMP) express the calcitonin-receptor protein, being one essential component of functional amylin receptors. Former experiments suggested that the dopaminergic system is involved in amylin's effect via D2 receptors. We now show that the pertinent receptors may be involved in signal transmission from the AP to the nucleus of the solitary tract (NTS) since local infusion of a D2 antagonist (raclopride, 10 micro-g/rat) into the AP/NTS region blocked peripheral amylin's effect. The involvement of the dopaminergic system in this region in amylin's effect is supported by immunohistochemical studies showing a marked overlap of cells with amylin-induced c-fos expression and cells expressing tyrosine hydroxylase (TH), the rate-limiting enzyme in dopamine synthesis (double labeling for c-fos in more than 90 % of TH-+ cells). The central pathways mediating amylin's anorectic action may therefore involve an activation of amylin receptors in the AP and signal transmission via dopaminergic neurons and D2 receptors in the AP/NTS region. Interestingly, CCK's anorectic action, which at least partly depends on endogenous amylin, also involves dopaminergic transmission in this brain region. Therefore, the dopaminergic system might be involved in integrating CCK and amylin signaling.

Feeding Strategy in Rats offered a Choice between pure Proteins and a Carbohydrate-Lipid Mix. L. MAKARIOS LAHHAM, S. ROSEAU, D. TOME, P. EVEN, *INRA, INA-PG, 16 rue Claude Bernard, 75005, Paris , France.*

When rats are offered a choice between the three macronutrients they often ingest up of 50% of their caloric intake protein. To better understand the rational for this apparently paradoxical choice, we have analyzed the pattern of feeding of rats who could select spontaneously from two food cups, one with pure proteins, the other with a mix of carbohydrate (HCHO) and lipid equivalent to the one in the maintenance diet. As soon as the first day of choice, protein intake amounted 35% of the caloric intake and then increased further to reach 51% on day 14. 70% of the caloric intake occurred under the form of mixed meals that in most cases (70%) were terminated by the ingestion of proteins. In addition, it was observed that food intake during the light period decreased from 40% to 10% of the daily caloric intake, and that most of the intake was in the form of meals of pure proteins. It is concluded that when rat can select their proteins independently, they can adopt a specific feeding strategy that allows them to adapt to the underlying metabolic transitions occurring during the day/night cycle. This probably

favors the ingestion of amounts of proteins that would be inadequate or less well accepted if given in a monotonous diet.

Adaptation to high protein diet involves both nitrogen and carbohydrate metabolism in rat. L. MAKARIOS LAHHAM, S. ROSEAU, J.-C. BOUTHEGOURD, D. TOME, P. EVEN, *INRA, INA-PG, 16 rue Claude Bernard, 75005, Paris, France.*

Post prandial changes in glucose, lipid and protein oxidation have been measured in rats by means of continuous measurement of respiratory exchanges and urea production on days 1, 4, and 15 of adaptation from a 14% (P14) to a 50% (P50) protein diet. The thermogenic response to the first P50 meal was strongly reduced as a result of a late increase in post-prandial protein oxidation (Pox), indicating that TEF depression was mainly due to an incapacity to oxidize the large flow of amino acids brought by this first P50 meal. On day 4, TEF was still depressed, but in contrast to day 1, Pox was strongly increased at the expense of a reduced post-prandial increase in glucose oxidation (Gox). On day 15, the rats were apparently adapted to the P50 diet. It is concluded that during adaptation to a high protein diet, the priority is given to the handling of the amino acids brought by the meal that is permitted by a transient decrease in the post-prandial oxidation of the carbohydrates.This process is probably the resut of a competition between carbohydrates and amino-acids as glucose precursors and lasts about 15 days before the liver is able to adapt the synthesis of both glucose and glycogen to the new amino-acids/carbohydrate mix brought by the high protein diet.

Estradiol inhibits real feeding, but not sham feeding, of corn oil emulsions in ovariectomized rats. M. MANGIARACINA, N. GEARY, *Bourne Laboratory, NY Presbyterian Hospital-Weill Cornell Medical College, White Plains, NY 10605, USA.*

Estradiol (E2) decreases meal size, food intake and body weight in ovariectomized (OVX) rats. Here we evaluated the relative contributions of oral and post-oral food stimuli generated by ingestion of corn oil to E2's meal size effects. OVX Long-Evans rats were implanted with gastric sham-feeding cannulas or left uncannulated. Half of each surgical group was subcutaneously injected once each 4th d oil-treated rats' body weights stabilized 30-40 g more than E2-treated rats. After overnight chow deprivation, rats sham or real fed 6.25% or 25% emulsions of corn oil in distilled water plus 0.75% Tween 80. Rats were tested every 2nd d, immediately pre-injection and 2 d post-injection, modeling diestrus and estrus, respectively, in E2-treated rats. As there were no cyclic effects, only "estrus" data are reported. E2-treatment significantly decreased real intake of 6.25% (Oil, 4.4 ± 0.5 vs. E2, 2.2 ± 1.0 ml/45 min) and 25% (3.0 ± 0.2 vs. 0.4 ± 0.3) corn oil, but E2 had no significant effect on sham intake of corn oil (6.25%: 18.2 ± 3.3 vs. 13.6 ± 3.5; 25%: 17.2 ± 3.6 vs. 18.3 ± 4.3). These data indicate that E2 reduces ingestion of corn oil emulsions, that post-oral food stimuli are necessary for this inhibition, and that orosensory food stimuli are not sufficient for it. These data match previous work with sucrose solutions (Appetite 37:150, 2001). Supported by DK54523.

Feeding and c-Fos activation in response to urocortin administration in intact and chronic decerebrate rats. S. MARKISON[1], D. DANIELS[2], H.J. GRILL[1], J.M. KAPLAN[1], *University of Pennsylvania, Dept. of Psychology[1] and Animal Biology[2], Philadelphia, PA 19104, USA.*

Urocortin (UCN), a member of the corticotropin releasing factor family of peptides, has been shown to play a role in the regulation of food intake and energy balance. UCN and its receptors (CRF-R1 and CRF-R2) are widespread throughout the brain and prominent in the hypothalamus and brainstem. We have begun to investigate the contribution of the brainstem to UCN's effect on feeding using the chronic decerebrate (CD) rat preparation. In the first experiment, feeding behavior was examined by measuring intraoral intake of a 12.5% glucose solution infused into the mouth (1 ml/min) after fourth ventricular treatment of 3.0 mg UCN or 3 ml aCSF. UCN suppressed intake in both CD (n=9) and control (n=7) rats ($p<0.001$). In an attempt to determine what areas of the brain are activated by UCN and, therefore, may mediate the effects of UCN on ingestive behavior, we also quantified c-fos immunohistochemistry in the paraventricular nucleus (PVN), the parabrachial nucleus (PBN), the rostral ventrolateral medulla (RVLM), and the nucleus of the solitary tract (NTS). Not surprisingly, c-fos activation anterior to the transection (i.e., PVN) was present in intact, but not CD rats. Within the brainstem, intact rats showed UCN-induced c-fos expression in the NTS, PBN, and RVLM. In CDs, c-fos was induced by UCN in the NTS, but not at all in the PBN and not significantly in the RVLM. The results suggest that a portion of the caudal brainstem is sufficient for the stimulation and mediation of UCN-induced anorexia. NIH: F32-DK 60547, R01-DK-21397, R01-DK 42284.

The impact of meal size and body size on individuals' perceptions of males and females. Y. MARTINS[1], P. PLINER[2], *[1]Monell Chemical Senses Center, Philadelphia PA 19104, USA; [2]Department of Psychology, University of Toronto at Mississauga,Mississauga, Ontario, Canada, L4L 1C6.*

Male and female participants provided impression ratings for either a normal weight or overweight male or female target who was portrayed as eating either small meals or large meals. Males rated normal weight targets as more physically attractive than overweight targets whereas ratings of physical attractiveness were unaffected by the body size manipulation amongst female participants. In addition, among male targets, the overweight large eater was rated the least socially attractive. For female targets, males rated the normal weight large eater as the most socially attractive, whereas females rated the normal weight small eater as the most socially attractive. These results are somewhat inconsistent with our previous understanding of how body size and meal size interact to affect impressions of others and may be reflective of a social change in this area.

The nociceptin-orphanin FQ/NOP receptor system as a target for treatment of alcohol abuse. M. MASSI, R. CICCOCIOPPO, A. FEDELI, C. POLIDORI. *Dept. of Pharmacological Sciences and Experimental Medicine, University of Camerino, 62032 Camerino (MC), Italy*.

Studies of our group have shown that intracerebroventricular (ICV) treatment with the 17 aminoacid peptide orphanin FQ/nociceptin (OFQ/N), the endogenous ligand of the NOP receptor (previously referred to as ORL-1 or OP4 receptor), reduces voluntary 10% ethanol intake in genetically selected Marchigian Sardinian alcohol-preferring (msP) rats (1). Studies aimed at the pharmacological characterization of the receptor which mediates the effect have shown that the C-terminal 13 aminoacid sequence is crucial for activity and that the selective NOP receptor antagonist [Nphe1]NC(1-13)NH2 is able to block the effect of OFQ/N on ethanol drinking. In place conditioning studies, OFQ/N abolishes the conditioned place preference induced by ethanol in msP rats, or by morphine in non selected Wistar rats; these findings suggest that OFQ/N is able to abolish the rewarding properties of ethanol and morphine. In addition, OFQ/N reduces the oral self-administration of 10% ethanol under an FR1 schedule of reinforcement in msP rats. Lastly, in relation to its antistress properties OFQ/N is able to abolish reinstatement of alcohol-seeking behavior following exposure to stress induced by electric foot-shock (2). Together, these findings suggest that OFQ/N and its receptor may represent an interesting target for pharmacological treatment of alcohol abuse. References 1. Ciccocioppo et al., (1999) Psychopharmacology 141: 220-224. 2. Martin-Fardon et al., (2000) NeuroReport 11: 1939-1943.

Lesions of the subfornical organ reduce the expression of calcium appetite by calcium-deprived rats. S.A. MCCAUGHEY[1], D.A. FITTS[2], M.G. TORDOFF[1], [1]*Monell Chemical Senses Center, Philadelphia, PA 19104; [2]Dept. of Psychology, University of Washington, Seattle, WA 98195, USA.*

Calcium-deprived rats develop a compensatory appetite for substances that contain calcium. Little is known about which brain areas control this behavior, although the subfornical organ (SFO) is likely to be important. The SFO contains a high density of calcium-sensing receptors and is known to influence ingestive behaviors such as thirst and sodium appetite. We used electrolytic lesions of the SFO to investigate its role in calcium appetite. Subjects were male Sprague-Dawley rats. They were maintained on a low-calcium diet (25 mmol/kg Ca++) for four weeks, after which they received either real or sham lesions of the SFO. Four days later, intakes of 30 mM CaCl2 and water were measured for 24 h in a two-bottle test. Subjects were considered to be SFOX if at least 90% of the SFO, including the rostroventral stalk, was destroyed. SFOX rats (n = 11) had significantly lower CaCl2 intakes than did rats with sham lesions (n = 11) at 60 and 120 min. The two groups had similar plasma ionized calcium levels on the day of behavioral testing. Most likely, the SFO is one of several brain regions that are sensitive to the effects of calcium deprivation and that act to stimulate calcium intake in deprived rats. This work was supported by NIH grant DK10134.

Peripheral doses of the dopamine 3 receptor agonist, 7-OH-DPAT, differentially reduce food intake in an ad libitum versus meal feeding paradigm. J.-A. MCQUADE, S.C. BENOIT, S.C. WOODS, R.J. SEELEY, *Dept. of Psychiatry, University of Cincinnati, Cincinnati, OH 45267-0559, USA.*

Mesolimbic dopaminergic system activation follows ingestive behavior in numerous paradigms and DA release is enhanced by ingestion of highly palatable diets. The dopamine-3 receptor (D3-R) has a limited expression pattern that is restricted largely to the mesolimbic dopaminergic system. The D3-R has been hypothesized to inhibit DA-mediated reward, locomotion and motivation. To test the potential for an inhibitory role of the D3-R on food intake, we administered peripheral 7-OH-DPAT (5, 10, 50 ìg/kg) to rats that had ad libitum access to

standard rodent chow (3.41 kcal/gm, 0.51 kcal/gm from fat) or a high-fat, palatable diet (4.4 kcal/gm, 1.71 kcal/gm from fat). In the chow group percent suppression relative to saline was: 5 µg/kg (30 min: 132 ± 31.8, 1 hour: 125 ± 19.6), 10 µg/kg (30 min: 82.7 ± 16.4, 1 hour: 98.3 ± 13.2), and 50 µg/kg (30 min: 84.7 ± 15.4, 1 hour: 93.0 ± 13.1). In the high fat group percent suppression relative to saline was: 5 µg/kg (30 min: 103.6 ± 22.5, 1 hour: 75.5 ± 6.23), 10 µg/kg (30 min: 76.5 ± 21.3, 1 hour: 62.0 ± 10.1), and 50 µg/kg (30 min: 100.8 ± 26.2, 1 hour: 64.3 ± 6.85). ANOVA did not reveal a diet x drug interaction. However, there was a main effect of drug $F(2,36) = 6.23$, $P < 0.05$. In the second set of experiments we administered 7-OH-DPAT (10, 50, 100 ìg/kg) to rats that had access to chow or high-fat diet for only 3 hours per day (meal fed). In the chow group percent suppression relative to saline was: 10 µg/kg (30 min: 101 ± 8.61, 1 hour: 93.0 ± 6.51), 50 µg/kg (30 min: 65.0 ± 10.7, 1 hour: 61.8 ± 6.26), and 100 µg/kg (30 min: 37.3 ± 3.92, 1 hour: 43.6 ± 3.33). In the high fat group percent suppression relative to saline was: 10 µg/kg (30 min: 92.2 ± 9.41, 1 hour: 94.0 ± 9.53), 50 µg/kg (30 min: 55.3 ± 10.8, 1 hour: 65.6 ± 11.4), and 100 µg/kg (30 min: 41.4 ± 4.10, 1 hour: 45.3 ± 4.05). ANOVA did not reveal a diet x drug interaction. However, there was a main effect of drug $F(2,36) = 46.91$, $P < 0.05$. These data suggest that when rats are restricted to a meal feeding paradigm, 7-OH-DPAT, is more efficacious in reducing food intake. Additionally, the reduction of food intake is not dependent on the palatability of the diet.

Restraint and disinhibition are related to psychopathology in morbidly obese patients seeking bariatric surgery. V. MOIZE[1], JM. PERI[2], B. SUREDA, R[2]. MORINIGO[1], C. YOLDI[1], J. VIDAL[1]. [1]*Unit of Obesity, Endocrinology Dept.,* [2]*Psychology Dept., Hospital Clinic, Barcelona, Spain.*

Some psychological complications have been seen after gastric surgery (Guisado JA, 2002). Patients that have to go thru it need to be screened before treatment in order to identify the factors that may lead to psychiatric complications. We evaluated behavioral and psychological aspects in 74 obese individuals (59 f, 15 m) presenting to our clinic for bariatric surgery. Patients (age=46.4+11.5y; BMI= 45.5+6.1 kg/m2) completed the Three Factor Eating Questionnaire [TFEQ Spanish version] and the Mini-Mult test (MMT) to assess psychopathology, and were interviewed to assess the presence of binge eating. Fifteen percent were binge eaters, and they had higher total TFEQ scores ($p<.05$), but not MMT scores (p = n.s.). Binge eaters had higher for disinhibition ($p<.02$) and psychasthenia ($p < .02$), scores compared to non- bingers. There were no differences in the TFEQ total scores in patients grouped as either high or low scorers on the MMT (p = n.s). Total TFEQ and MMT scores did not differ by gender, but women and scored higher for restraint and hypochondriacs than men ($p<0.05$). Restraint was inversely related with BMI, ($p<.05$) and with mania ($p<.001$), and disinhibition was associated with depression ($p<.05$) and psychasthenia ($p<.05$). Patients with BMI< 40 (n=12) showed higher total TFEQ scores ($p<.05$) than those with BMI > 40. In conclusion, disinhibition is higher in binge eaters and low restraint is related to increased obesity. In morbidly obese patients, disinhibition appears more important in binge eaters who also show high score of psychasthenia and depression.

Conditioned increase in acceptance and preference, but not palatability of sour or bitter tastes paired with intragastric glucose infusions. K.P. MYERS[1,2], A. SCALFANI[2], *Dept. of Psychology,* [1]*Bucknell University, Lewisburg, PA 17837, and* [2]*Brooklyn College of CUNY, Brooklyn, NY 11210, USA.*

Rats learn strong preferences for tastes or flavors paired with the postingestive effects of glucose. We found that a sweet CS+ flavor paired with intragastric (IG) glucose subsequently elicited more hedonic taste reactivity (TR) responses than a sweet CS- paired with IG water (Myers & Sclafani 2001). Here we determined if a glucose-conditioned preference for a sour or bitter taste, which are avoided by naive rats, would also elicit hedonic TR responses. Rats were trained 20 hr/day and then 30 min/day with one taste (CS+; citric acid or sucrose octaacetate) paired with IG glucose (16%), and the opposite taste (CS-) paired with IG water. Conditioning substantially increased CS+ acceptance and preference, relative to CS-, as measured in one- and two-bottle tests. However, TR responses to intraoral infusions of the CS+ and CS- did not differ, even after extensive testing. In subsequent two-bottle tests, rats preferred 1% fructose to the CS-, but the CS+ to 1% and 2% fructose. They equally preferred the CS+ to 4%, 8%, and 16% fructose, which contrasts with prior data showing a sweet CS+ is preferred to 4% and 8% fructose and isopreferred to 16% fructose. These results suggest that a conditioned preference for a bitter or sour CS+ is accompanied by minimal change in CS+ palatability, and a non-hedonic process, perhaps increased incentive salience, is responsible for the enhanced CS+ preference and acceptance. Supported by NIH grants CD00444 and DK31135.

The relationship between self-reported eating behavior and performance in a behavioral task assessing food reinforcement. J.A. NASSER, S.M. EVANS, R.W. FOLTIN, *New York State Psychiatric Institute and Columbia University, New York NY 10032, USA.*

This pilot study used a non-clinical human sample to begin examining the relationship between food reinforcement and self-reported eating behavior. Four men and 11 women (22 to 43 years of age), with BMI's ranging from 20 to 40, participated in a single test session. Each participant completed the Three Factor Eating Questionnaire (TFEQ) and the Gormally Binge Eating Scale (BES). BES scores ranged from 0 to 13 (normal < 17). Food reinforcement was assessed using a 10-min progressive ratio task performed 15 minutes after participants consumed 300 kcal of pudding. Responses for the 10-trial task varied from 10 to 190. Participants chose between food and non-food items (of equal monetary value) at each trial. Food Break Point (FBP, the highest ratio of responses completed for food items) served as the measure of salience of the food items, and ranged from 0 to 190. BES scores were significantly correlated with body weight ($r = 0.8$, $p < .001$), BMI ($r = 0.7$, $p = .002$) and TFEQ-D ($r = 0.5$, $p < .03$). FBP was not correlated with BMI or TFEQ-D. A positive trend was observed between FBP and BES score ($r = 0.4$, $p = .07$) and body weight ($r = 0.4$, $p = .07$). These data suggest that ratings of self-reported eating behavior can be related to performance on a task assessing food reinforcement. This task may be useful for studying various conditions that promote binge eating. Supported by NIH grant DA 09236.

Melanocortin receptors couple to multiple signal transduction pathways in cultured cells. C.S. PATTEN, L.N. WEINBERGER, D. DANIELS, M.A. KUHN, J.D. ROTH, J. HINES, D.K. YEE, S.J. FLUHARTY, *Depts. of Animal Biology and Pharmacology, Biological Basis of Behavior Program, and Institute of Neurological Sciences, University of Pennsylvania, Philadelphia, PA 19104, USA.*

Central administration of melanocortin agonist, a-MSH or MTII, significantly decreases, while their endogenous antagonist, agouti-related peptide (AgRP), increases food intake. These changes can last for several days suggesting long-term changes in cellular signaling and gene expression. Because we reported previously that murine N1E-115 neuroblastoma cells contain mRNA for proopiomelanocortin (POMC), AgRP and only two subtypes of melanocortin receptors, MC3-R and MC4-R, we used these cells to explore the biochemical actions of melanocortins in vitro. Consistent with the known coupling of MC3-R and MC4-R with Gs and not Gq, activation of these receptors with the agonist a-MSH produced dose-dependent increases in cAMP levels but did not alter phosphoinositide hydrolysis. More significantly, we also found that activation of these receptors with a-MSH (1 μM; 10 min) stimulated phosphorylation and activation of p42/p44 mitogen-activated protein kinase (MAPK), a diverse signal transduction pathway directly involved in transcription. Since N1E-115 cells possess both MC3-R and MC4-R, and a-MSH is a non-selective agonist, we used transfected COS cells and the selective agonist MTII, to determine the receptor subtype mediating this response. MTII increased MAPK phosphorylation in MC4-R-transfected COS cells but was ineffective in cells transfected with MC3-R or in non-transfected controls. Collectively, the present data suggest that MC4-R activation can stimulate phosphorylation of MAPK in neuron-like cells. It remains to be determined if this signal transduction pathway is involved in the long-term behavioral actions of melanocortins or their endogenous antagonist, AgRP. Supported by NIH grants MH 43787, DK 50218, and HL 58792.

Pro-orphanin FQ/nociceptin mRNA and NOP receptor mRNA levels in the forebrain of food-deprived rats. C. POLIDORI, M. SIMONATO, M. MASSI, *Dept. of Pharmacological Sciences and Experimental Medicine, University of Camerino, 62032 Camerino, Italy, and Dept. of Pharmacology, University of Ferrara, 44100 Ferrara, Italy*

Forebrain injections of orphanin FQ/nociceptin (OFQ/N), the endogenous ligand of the NOP opioid receptor, previously referred to as ORL1 or OP4 receptor, stimulates feeding in freely feeding rats. The NOP receptor antagonist [Nphe1]OFQ/N(1-13)NH2 inhibits food deprivation-induced feeding. To further evaluate whether the OFQ/N-NOP receptor system plays a physiological role in feeding control, the present study evaluated forebrain levels of mRNA for the OFQ/N precursor (ProOFQ/N), as well as for the NOP receptor in food deprived rats. The results obtained show that food deprived rats have lower mRNA levels for the NOP receptor in several forebrain regions; a significant reduction was found in the paraventricular and lateral hypothalamic nuclei and in the central nucleus of the amygdala. Moreover, food deprived rats exhibited lower mRNA levels for the Pro-OFQ/N in the central amygdala. These findings, together with the observation that NOP receptor antagonists reduced food deprivation-induced feeding, suggest that this system may have a physiological role in feeding control. The observation that food deprivation reduces the gene expression of the OFQ/N-NOP receptor system is apparently not consistent with a direct hyperphagic action for OFQ/N. In keeping with the notion that OFQ/N exerts inhibitory actions at cellular level, the present results may be consistent with the hypothesis that OFQ/N stimulates feeding by inhibiting neurons inhibitory for food intake; in conditions of food deprivation these neurons may be silent and also the OFQ/N-NOP receptor system, which controls them, may be regulated at a lower level.

Central injections of leptin reduce food intake, but not ethanol intake in Marchigian Sardinian alcohol-preferring (msP) rats. C. POLIDORI, L. FOSCOLO, F. LUCIANI, R. CICCOCIOPPO, N. GEARY[1], M. MASSI, *Dept. of Pharmacological Sciences and Experimental Medicine, University of Camerino, 62032 Camerino, Italy; [1]Bourne Laboratory, NY Presbyterian Hospital, Weill Medical College of Cornell University, NY 10605, USA.*

Presbyterian Hospital-Weill Cornell Medical College, White Plains, NY 10605 USA. Leptin reduces food intake in rats (1). To evaluate whether it also reduces ethanol intake, acute or chronic leptin treatments were given to msP rats, by injections into the third cerebroventricle (3V). They were offered daily access to 10% ethanol (ETOH) 2 h/day, at the beginning of the dark period of a 12:12 light/dark cycle. In the acute study rats (n=6) received injection of saline or leptin 1-8 mg/rat 1 h before ETOH access and their intake was recorded at 30, 60 and 120 min. In the chronic study 2 groups of 9 rats were used. The first received injection of vehicle 1 m l/rat, while the second received leptin 8 m g/rat 1 h before ETOH access for 9 consecutive days. Ethanol intake was recorded after 2 h; food intake was recorded together with ethanol, as well as at 24 h after injection. Acute injection of leptin did not modify ethanol intake (1.32 +/- 0.16 g/kg after vehicle versus 1.25 +/- 0.2 after leptin 1 m g/rat and 1.49 +/- 0.24 g/kg after leptin 8 m g/rat); the dose of 8 m g/rat of leptin significantly reduced food intake at 24 h, but not at 3 h postinjection. In the chronic study leptin, 8 m g/rat, significantly ($P<0.01$) reduced food intake by about 30-50%, but did not modify ethanol intake. The results obtained indicate that leptin selectively reduces food intake leaving unaltered ethanol intake in msP rats. (Supported by NIAAA grant # 1R21AA12880-01) References 1) Schwartz MW et al.. J Clin Invest. 1996; 98:1101-6.

Analysis of orexigenic mRNAs by RNAse Protection Assay. J.A. REED, D.J. CLEGG, R.J. SEELEY, *Obesity Research Center; University of Cincinnati; Cincinnati, OH 45223, USA.*

Analysis of changes in mRNA abundance following experimental manipulation has been of great interest in the study of food intake and body weight regulation. While in situ hybridization allows one to determine the spatial and temporal fluctuations in mRNA expression, it has limitations when used as a quantitative measure or to measure multiple mRNA species of interest. Semi-quantitative RT-PCR provides a relative measure of mRNA abundance, but does not allow one to easily measure multiple mRNA species in the same reaction mixture. We have developed an array of probes for use in the RNAse Protection Assay (RPA) to measure expression of genes known to mediate energy homeostasis in the rat. RPA allows detection of relative abundance of multiple mRNA species simultaneously in a single reaction. PCR-generated fragments of rat genomic DNA or cDNA were used as templates in the development of some probes, while others were subcloned fragments of cDNAs previously used as in situ probes. Hybridization conditions were empirically determined to produce a multiplexed RPA for rat NPY, AgRP, and orexin mRNAs, with GAP-DH as a control. This assay is a sensitive and highly specific measurement of gene expression, and allows us to precisely identify changes in mRNA accumulation that are coordinately regulated in response to homeostatic disruptions.

Changes in test meal size and metabolic abnormalities in response to a carbohydrate preload following liver transplantation. P.J. REGAN[1], H.I.M DAVIDSON, R.A. RICHARDSON, O.J. GARDEN, W. LANGHANS[2], *[1]Dept. Dietetics, Nutrition & Biological Sciences, Queen Margaret University College, Edinburgh Lothian EH12 8TS, Scotland, [2]Institute of Animal Sciences, Swiss Federal Institute of Technology, 8603 Schwerzenbach, Switzerland.*

The liver and its innervation have been implicated in the control of ingestive behaviour. This study assessed food intake and subsequent metabolic changes after a pure carbohydrate (CHO) preload in liver (LTx) and renal (RTx) transplant recipients and controls. Fasted subjects were given the CHO preload (250kcal) and 45 minutes later offered a test meal (pasta and sauce). Metabolic measurements included energy expenditure, plasma glucose, insulin and lactate. Results post meal were normalised and expressed as AUC per gram of CHO consumed at the meal (mean ± SEM). Test meals (g/lean body mass) were smaller but insulin responses were significantly higher in the LTx group (238.24 ± 60.03) than RTx group (60.18 ± 7.63) ($p<0.05$, LTx v RTx) but not controls (133.56 ± 27.02). LTx group exhibited higher glucose (36.15 ± 8.38) values compared to RTx (13.74 ± 2.26) and controls (17.03± 2.77) although this failed to reach significance ($p=0.058$). Lactate response in LTx was consistently higher (4.153 ± 0.813) than RTx (1.876±0.288) and controls (3.355 ± 0.607) but did not reach significance. Energy expenditure was related to lean body mass and results indicated no statistical differences between LTx (59.81 ± 12.17), RTx (26.79 ± 2.63) and controls (39.79 ± 6.87). These results suggest that the satiating potency of CHO in LTx is enhanced and gram for gram CHO eaten they show an abberant

metabolic response to feeding which may be a consequence of hepatic denervation and altered autonomic integration following ingestion.

Postnatal development of vagal-hypothalamic pathways. L. RINAMAN, *Dept. of Neuroscience, University of Pittsburgh, Pittsburgh, PA 15260, USA.*

Physiological, behavioral, and anatomical evidence will be presented to demonstrate the functional maturation of ascending and descending neural connections between hindbrain vagal sensory/motor areas (dorsal vagal complex, DVC) and the hypothalamus in rats. The postnatal development of these pathways provides the opportunity to correlate developmental events in their formation with the postnatal emergence of mature homeostatic responses to interoceptive stimuli. For example, in adult rats stimulation of vagal gut afferents with CCK activates DVC neurons, and activates hypothalamic magnocellular and parvocellular neurons. Conversely, CCK treatment in neonatal rats activates the DVC but fails to activate the hypothalamus, and fails to increase plasma levels of oxytocin or ACTH. As a second example, plasma hyperosmolality in adult rats activates both hypothalamic and DVC neurons, and inhibits gastric emptying and food intake (dehydration anorexia). In contrast, although hyperosmolality in neonatal rats robustly activates the hypothalamus, few DVC neurons are activated, and neither gastric emptying nor food intake are inhibited. These findings can be interpreted in the context of anatomical data revealing a gradual postnatal maturation of ascending inputs from the DVC to the hypothalamus, and of descending inputs from the hypothalamus to the DVC. Research supported by NIH grant #MH01208.

The influence of meal palatability on intestinal control of feeding and appetite. T.M. ROBINSON[1], S.J. FRENCH[1], R.W. GRAY[2], M.R. YEOMANS[2], *[1]Centre for Human Nutrition, University of Sheffield, Sheffield, S5 7AU: [2]Experimental Psychology, Sussex University, Brighton, UK.*

This study investigated the effects of intra-intestinal infusions of low- (63 kcal) or high-energy (360 kcal, Fat) soup on subsequent food intake and appetite when subjects were given meals of different palatabilities. Male volunteers consumed either a bland or a palatable pasta and tomato sauce meal 30 minutes following the end of a 300 ml infusion of soup into the duodenum. Food intake and rated appetite during the test meal were recorded continuously using a modified universal eating monitor and custom software. Preliminary results suggested that a high-energy content soup significantly reduced test meal intake ($p < 0.05$) by approximately 35 kcal in both palatable and bland meal conditions. A non-significant trend ($p = 0.1$) was seen for greater intake when the test meal was palatable. High energy preloads reduced initial hunger at the start of the test meal ($p = 0.01$), however hunger was stimulated at this time when the meal was palatable ($p < 0.05$). A similar, although non-significant, trend for fullness was observed, with greater fullness following high energy preloads ($p = 0.07$) and a reduction in fullness when a palatable meal was given ($p = 0.07$). These preliminary data suggest that intestinal signalling mechanisms may account for only a small part of the feedback control of eating and, possibly, that variations in food palatability may influence this feedback to reduce this control further. Further data, including energy intake over the remainder of the day will also be discussed.

Effects of intragastric infusions of glucose, polycose, peptone, 80% polycose/20% peptone, oleic acid, Intralipid, and corn oil on food intake and meal patterns in rats. E. ROLF, R.D. REIDELBERGER, *VA Medical Center, Omaha, NE 68105, USA.*

The relative effectiveness of equicaloric amounts of dietary fat versus other macronutrients in producing satiety remains controversial. This study compared the effects of intragastric infusions of glucose, polycose, peptone, 80% polycose/20% peptone, oleic acid, Intralipid, and corn oil on food intake and meal patterns in rats. Non-food deprived rats (n=11-15) received a 2-h intragastric infusion of macronutrient beginning 15 min before dark onset. Doses ranged from 1.25 to 10 kcal/h except for corn oil, which was delivered at 2.5 to 20 kcal/h. Chow intake and meal patterns were recorded for 17 h after infusion onset. Each macronutrient inhibited food intake dose-dependently during the first 4 h. All non-fat infusates had a similar potency and efficacy, with food intake returning to normal within 2 h of the end of infusion. Intralipid, an emulsion containing long-chain triglycerides, was significantly less efficacious than the non-fat nutrients. Corn oil was also less efficacious during the initial 2 h, but produced a more-prolonged response, such that by the end of the 4-h period, corn oil exhibited a potency and efficacy similar to that of the non-fat nutrients. Oleic acid, a long-chain fatty acid emulsion, was the most potent inhibitor of food intake. However, oleic acid also decreased rate of eating within meals suggesting that it may have produced malaise or discomfort. These results suggest that dietary fat, which like corn oil consists largely of unemulsified long-chain triglycerides, is as satiating as dietary carbohydrate and protein. Supported by NIH-DK55830 and Dept. of Veterans Affairs.

Environmental influences on eating behavior: portion size and energy density. B.J. ROLLS, *Nutrition Dept., The Pennsylvania State University, University Park, PA 16802, USA.*

Energy intake depends upon an interaction of physiological, behavioral and environmental influences. With the rapid rise in the incidence of obesity the importance of environmental influences on intake is evident. In particular, the wide availability of a variety of inexpensive, energy-dense, palatable foods in large portions may promote overeating. Recent studies indicate that young children appear to eat in response to physiologic cues while older children learn to eat in response to environmental cues such as portion size. Thus, in both older children and adults, the bigger the portion served the greater the energy intake. This response to portion size was seen with different types of foods (macaroni, sandwiches, potato chips). Subject characteristics such as sex, body weight, restraint, or tendency to clean the plate did not affect the response to portion size. Studies on the influence of the energy density of food suggest one possible strategy to limit the impact of portion size on energy intake. When the palatability of different versions of a food was matched but energy density was lowered by as much as 30%, subjects ate a consistent weight of food and thus spontaneously ate 30% less energy. Despite the reduction in intake, they reported feeling just as full. Thus, one way to limit the effect of large portions on energy intake is to lower the energy density of the food. To be accepted by the consumer, reductions in energy density should minimally affect the palatability and cost of the food. (Support DK39177 & DK59853)

In Utero Development of Thirst and Appetite: Neuronal and Physiologic Correlates. M.G. ROSS, *Harbor UCLA Med. Center, Dept. of Ob-Gyn, Torrance, CA 90509, USA.*

Fetal swallowing occurs in utero, serving to regulate amniotic fluid volume and aid in gastrointestinal tract development. Disorders of fetal swallowing may result in either deficient or excess amniotic fluid (oligohydramnios or polyhydramnios, respectively). These amniotic fluid volume disturbances may have serious consequences on the outcome of the pregnancy. Our perinatal laboratory at Harbor-UCLA has explored the development of ingestive behavior in a novel, chronically instrumented ovine fetal preparation. We have demonstrated that the near term ovine fetus swallows at a rate of 100-300 ml/kg which is markedly greater, per body weight, than that of the adult (40-60 ml/kg). This high rate of fetal swallowing is likely maintained via overexpression of angiotensin-II and glutamate N-methyl-D-aspartate receptors and nitric oxide synthase within the hypothalamus. Near term fetal ingestive behavior is stimulated in response to putative dipsogenic factors, evidenced by increased swallowing and Fos staining in select hypothalamic nuclei (i.e., SFO, MnPO, OVLT). In addition to “thirst”-mediated responses, near term ovine fetal appetite may be stimulated by oral sucrose infusion and by central injection of the orexic protein neuropeptide-Y. However, leptin, which has an appetite inhibitory effect in the adult, increases, rather than suppresses, fetal swallowing. We propose that unopposed appetite stimulatory mechanisms induced by the orexic protein neuropeptide-Y during the newborn period may facilitate rapid newborn weight gain despite high body fat levels. Understanding of the mechanism of fetal-neonatal appetite behavior may provide insight into the fetal programming of adult hyperphagia and obesity and provide for novel therapeutic approaches during pregnancy and the newborn period.

Expression, function, and regulation of insulin receptors in murine N1E-115 neuroblastoma cells. J.D. ROTH, L.N. WEINBERGER, J. HINES, D. DANIELS, D.K. YEE, S.J. FLUHARTY, *Depts. of Animal Biology and Pharmacology, Biological Basis of Behavior Program, and Institute of Neurological Sciences, University of Pennsylvania, Philadelphia, PA 19104, USA.*

Insulin plays a major role in several metabolic processes and has emerged as a candidate for central actions regulating food intake and body weight. Recently, we have reported that rt-PCR analysis of murine N1E-115 neuroblastoma cells detected mRNA for several neuropeptide receptors including insulin and insulin-like growth factor (IGF1). In the present experiments, Western blotting was used to demonstrate the presence of insulin- and IGF1-receptor in N1E-115 cells. Further analysis revealed that insulin receptor-immunoreactivity increased substantially during in vitro differentiation as the cells acquired a more neuron-like phenotype. This enhanced receptor expression was probably the result of increased gene transcription because it was accompanied by a parallel increase in insulin receptor mRNA levels as measured by Northern blot analysis. Moreover, activation of these receptors with insulin (1 mM; 10 min) stimulated phosphorylation (activation) of p42/p44 mitogen-activated protein kinase (MAPK). In view of the fact that N1E-115 cells also express leptin (OB-Rb) and corticosteroid (Type I) receptors, we examined the expression of insulin receptor in N1E-115 cells after overnight incubation with insulin (1 mM), leptin (50 ng) or dexamethasone (1 mM). Preliminary data indicate a strong effect of insulin or dexamethasone, but less of an effect of leptin. Collectively, these results suggest that N1E-115 cells may be a useful model in which to further investigate homologous and heterologous regulation of

insulin receptor expression and its cellular signaling within neuronal cells. Supported by NIH grants MH 43787, DK 50218, and HL 58792.

Characteristics of flavor avoidance in rats and mice compared using a non-deprivation protocol. N.E. ROWLAND, J. THOMAS, D.J. GREEN, K.L. ROBERTSON, *Psychology, Univ. of Florida, Gainesville, FL 32611-2250, USA.*

We have studied the formation of flavor avoidance using a protocol that is equivalent in both rats and mice and does not involve food or fluid deprivation. Animals are adapted to consuming a daily 30 min "dessert", which consists of 10% Polycose solidified in beakers or jars with gelatin and an added flavor as CS+. In a study in which LiCl (the US: 0.75 mEq/kg) was injected 1 hr after the dessert on 3 occasions, male rats showed a complete avoidance that was sustained for at least 6 extinction trials. Fewer injections of LiCl or a longer (5 hr) dessert-to-LiCl delay produced weaker and/or transient avoidance. In a discrimination protocol (in which the CS+ preceded LiCl and a CS- flavor preceded saline), rats showed substantial generalization of avoidance to the CS-. In contrast, in mice studied in a similar protocol (but using 3 mEq LiCl/kg and up to 6 pairings), avoidance of the CS+ was never complete and there was minimal generalization to the CS-. We found similar results using dexfenfluramine (DF)as US. Using similar dessert protocols, repeated administration of DF to rats was associated with rapid development of anorectic tolerance, but we have found no evidence for anorectic tolerance in mice. However, both species showed similar attenuations in brain Fos-ir induced by DF after chronic treatment. These data demonstrate robust species differences in associative or avoidance learning, and further suggest that tolerance to DF in rats may be primarily an associative learning effect.

Brain oxytocin blockade induces drinking and salt appetite. A.A. RUHF, D.A. FITTS, *Dept. of Psychology, University of Washington, Seattle, WA 98195, USA.*

A previous study demonstrated that an antagonism of brain oxytocin receptors with ornithine vasotocin [OVT, 10-µg, (d(CH2)5,Tyr(Me)2,Orn8-] exaggerated salt appetite after a lateral ventricular (icv) injection of angiotensin (ANG) II given 30 min later (Blackburn, Demko, Hoffman, Stricker, & Verbalis, Am. J. Physiol. 263, R1347-R1353, 1992). We repeated the Blackburn et al. experiment except that we allowed rats to drink water and 0.3 M hypertonic saline during the 30 min between icv injections of OVT and ANG II. OVT alone induced intake of water and saline solution (9.8 ± 1.2 and 4.3 ± 1.7 ml) compared with vehicle injection (1.1 ± 0.4 and 0.2 ± 0.1 ml). OVT-injected rats that later received ANG II did not show further exaggerated consumption, but this effect may have been blunted by the large volumes of water and salt already consumed. The data suggest that oxytocin exerts a tonic inhibition of both water and salt intake even in the absence of an ANG II stimulus.

Hyperphagia of mice lacking the bombesin receptor subtype-3 is characterized by increased meal size and decreased meal number. P. SANCHEZ, J. OVERDUIN, L. HAMTON, J. BATTEY, R. HENDERSON, J. GIBBS, *Bourne Laboratory, Weill Medical College of Cornell University, White Plains, New York 10605, USA.*

Mice with targeted deletion of the bombesin receptor subtype-3 (BRS-3) gene are hyperphagic and develop obesity (Ohki-Hamazaki et al, 1997; Overduin et al, 2001). We recorded body weight, food intake, and meal patterns (by lickometer) in BRS-3 gene-deleted mice from 24 to 61 weeks of age. Seven male BRS-3 deficient (-/Y) and 7 wild-type littermate controls (+/Y) were maintained on a balanced liquid food (1.4 kcal/ml) and water ad libitum. At 61 weeks, body weights were 54.5±2.3g for -/Y and 35.9±1.7g for +/Y mice (a 52% increase from +/Y mice; $p<0.001$), and daily food intake was 18.5±1.3ml for -/Y and 15.8±1.1ml for +/Y mice (a 17% increase; $p<0.03$). Mean daily meal number was 31.7±3.9 for -/Y and 43.3±2.5 for +/Y mice ($p<0.003$). Mean daily meal size was 734±39 licks for -/Y and 453±31 licks for +/Y mice ($p<0.000$). These data demonstrate that the hyperphagia of BRS-3 gene-deleted mice is characterized by increased meal size and decreased meal number. They are consistent with a role for bombesin-like peptides in the control of meal pattern, food intake, and body weight. (Supported by NIDDK RO1 DK 33248 and by the NIDCD).

Perception of food quantities by young women scoring high and low on the Eating Disorders. Inventory. M.L.S. SANTOS, P.P.P. MACHADO, *Dept. of Psychology, University of Minho, 4710-057 Braga, Portugal.*

Photographs of varied and quantified foods were shown to 32 young women. Participants had to indicate which were normal quantities that could be consumed by themselves and by other women of similar age. Also, excessive amounts for themselves and peers were asked. The body composition and demographic data were also obtained. Results were compared considering participants' scores on the Eating Disorders Inventory (EDI) and its subscales. The body composition and the Body Mass Index were significantly associated with the Bulimia and the Body dissatisfaction subscales. The body weight, the desired weight and the weight they thought they had were only significantly related to the Body dissatisfaction subscale. In general and in comparison with low scorers, high scorers presented a higher discrepancy between food amounts for themselves and for their peers. High scorers on EDI and the majority of its subscales reported for themselves less amounts of food than low scorers did. In contrast, these high scorers indicated for their peers more food than low scorers did. However, high Bulimia scorers reported for themselves than for their peers higher quantities of strawberry pie and cream cake. The present results suggest that women at-risk of developing an eating disorder, or with a high drive for thinness or not satisfied with their body image, tend to eat less than others, and believe their peers eat more than themselves. In contrast, there might be some foods consumed in higher quantities and possibly binged by women who score high on the Bulimia subscale.

Coping styles and insulin resistance. A.J.W. SCHEURINK, P.Y. WIELINGA, E.H.E.M. VAN DE WALL, L. BENTHEM, *Dept. of Neuroendocrinology, University of Groningen, PO Box 14, 9750 AA Haren, The Netherlands.*

Roman high- and low avoidance rats, selected for rapid versus poor acquisition of a two-way active avoidance response, differ in emotional reactivity and coping style. Roman low-avoidance rats (RLA) are highly emotional individuals with a passive coping style, whereas Roman high avoidance rats (RHA) behave as active copers with low emotional reactivity. The two selection lines are associated with particular neuroendocrine and neurochemical characteristics. RLA's show more pronounced emotional responses and markedly higher activation of the HPA-axis than RHA. Furthermore, differences between the two selection lines are reported for brain dopamine, CRH, serotonin and vasopressin.We investigated whether the two selection lines might be metabolically different. RLA's and RHA's were submitted to a series of intravenous glucose tolerance tests. RLA's were clearly insulin resistant in comparison to RHA's and control Wistars. Glucose tolerance was normal. RLA's are not overweight, which means that RLA's develop insulin resistance in the absence of obesity. We also gave RHA's and RLA's access to a highly palatable diet (85 % sweetened condensed milk + 15% cornoil) to test whether RLA rats were prone to diet-induced obesity. RLA-rats strongly prefered the high energy diet above chow and gained more weight than the RHA's combining their alleged insulin resistance with an increased susceptibility for diet-induced obesity. We suggest that the Roman Low Avoidance rat, a neurochemically and behaviorally well-documented selection line, may serve as (non-obese) rat model for studying the neurohormonal factors that may underlie the development of the metabolic syndrome and type 2 Diabetes.

Female rats, like male rats, exhibit individual differences in cocaine-induced avoidance of saccharin intake and greater avoidance of the tastant is associated with greater conditioned elevations in circulating corticosterone levels at test. P.L. SCHROY, E. LEUENBERGER, D.S. WHEELER, P.S. GRIGSON, *The Penn State College of Medicine, Hershey, PA 17033, USA.*

Despite the same number of saccharin-cocaine pairings, some male Sprague-Dawley rats (the Small Suppressers) exhibit a small reduction in intake of a saccharin conditioned stimulus (CS), while others exhibit a large reduction in CS intake (the Large Suppressers). The present experiment tested whether similar individual differences would be evident when using female Sprague-Dawley rats. During testing, water-deprived male and female rats were given 5 min access to 0.15% saccharin and, after a 5 min interstimulus interval (ISI), were injected with either a saline (n = 16/cell) or a cocaine (10 mg/kg sc) unconditioned stimulus (US) (n = 32/cell). There was one taste-drug pairing every 48 hr for 7 pairings followed by one saccharin CS only test. Plasma corticosterone (CORT) was evaluated 15 min after CS access both before and after the conditioning phase of the study. The results showed that Large and Small Suppressers were evident among both the males and the females. Furthermore, greater cocaine-induced suppression of CS intake was associated with higher CORT levels at test in both the males and females. Taken together, the data show that females, like males, also exhibit individual differences in avoidance of the saccharin CS following saccharin-cocaine pairings and greater avoidance of the saccharin CS cue is associated with higher levels of circulating CORT at test. Supported by NIH grants DA 09815, DA 12473 and F31 DA 15261-01.

Sweet taste facilitates flavor preference conditioning by intragastric fructose. A. SCLAFANI, K. ACKROFF, *Dept. Psychology, Brooklyn College of CUNY, Brooklyn, NY 11210, USA.*

Fructose, unlike glucose, has a weak postingestive reinforcing effect. In prior work, intragastric (IG) fructose infusions failed to condition a preference for nonsweet flavors (e.g., sour grape) in rats trained 22 hr/day. With other nutrients sweet taste can facilitate preference conditioning and this study determined if it would also enhance conditioning by IG fructose. Nondeprived male rats were trained to drink a CS+ flavor sweetened with 0.2% saccharin paired with IG fructose (16%), and a sweet CS- flavor paired with IG water. CS+ vs. CS- preference was assessed in a 2-bottle test. Other rats were trained and tested with nonsweet CS flavors. Rats tested with sweetened flavors preferred the CS+ to the CS- (74%), whereas rats tested with nonsweet flavors avoided the CS+ (36%). The rats drank more CS+ and were infused with more fructose when trained with sweet rather than nonsweet flavors. This does not readily explain, however, why fructose was aversive when paired with a nonsweet flavor. Some data suggest that saccharin facilitates preference conditioning by activating cephalic metabolic responses via the hepatic vagus. In a second experiment, however, hepatic vagotomy did not prevent rats from learning a preference for a sweet CS+ paired with IG fructose. These data indicate that a presumably unlearned response to sweet taste, perhaps mediated by other vagal branches, can substantially modify flavor-nutrient conditioning. Whether this is true of other inherently preferred tastes (polysaccharide, umami, fat) requires further study. Supported by NIH grant DK31135.

Molecular signaling in the anterior piriform cortex in response to corrected and threonine-devoid diets. J.W. SHARP, L.J. MAGRUM, C.M. ROSS, D.W. GIETZEN, *Dept. of Anatomy, Physiology, and Cell Biology, School of Veterinary Medicine, University of California, Davis, CA 95616, USA.*

The anterior piriform cortex (APC) is essential for recognition of indispensable amino acid (IAA) deficiency (DEF). We have shown that IAA DEF diets quickly activate APC neurons and induce translation of the immediate-early gene, c-fos. Increased calcium-mediated signaling was seen with IAA repletion in APC slices. Mitogen-activated protein kinase (MAPK) and calcium/calmodulin-dependent protein kinase II (CaMKII) were activated in response to IAA deficiency in the rostral APC. These kinases phosphorylate cyclic AMP-responsive element-binding protein (pCREB), a transcription factor for c-fos. Immunohistochemistry revealed increased pCREB after consumption of both corrected and threonine-devoid diets relative to the control diet. Phosphorylated CREB and c-fos were seen in many brain areas in rats fasted overnight, and then fed the experimental diets. Relative to other diets, rats fed threonine-devoid had significantly greater numbers of pCREB labeled nuclei in the rostral APC. Although primarily activated in APC, MAPK and CaMKII were not directly related to most pCREB/c-fos signaling. Less that half of the neurons with pMAPK labeling in the APC were also labeled for c-fos and most c-fos labeling was unrelated to MAP kinase. Little MAP kinase labeling occurred on other brain areas with c-fos expression. Therefore, increased c-fos translation after these diets may reflect two responses: 1) an initial wave of activation from the novel diet, 2) a specific molecular mechanism in the brain that detects IAA deficiency and activates MAPK and CaMKII systems resulting in c-fos translation 15 to 30 minutes after the initial wave of translation. (Supported by NIH-NS33347, DK337490 and USDA 2000-01049).

Sexual differentiation in the potency of bacterial lipopolysaccharide to inhibit feeding. J. SHEAHAN, L. ASARIAN, W. LANGHANS[1], N. GEARY, *Bourne Laboratory, NY Presbyterian Hospital-Weill Cornell Medical College, White Plains, NY 10605, USA, and [1]Institute of Animal Sciences, Swiss Federal Institute of Technology, 8603 Schwerzenbach, Switzerland.*

Lipopolysaccharide (LPS) causes anorexia during the acute phase response (APR) of the innate immune system that results from gram-negative bacterial infections. Because (a) immune function is sexually differentiated at molecular, physiological, and behavioral levels, and (b) estradiol increases the anorectic potency of LPS in ovariectomized rats (Geary, Nutrition 17:499, 2001), we compared the anorectic effects of LPS in intact male and female Long Evans rats. LPS (12.5 µg/kg) and saline vehicle were intraperitoneally injected at dark onset according to a crossover design, with 4 d separating trials, and spontaneous feeding was measured during the 12 h dark phase. Female rats were tested during estrus. LPS inhibited dark-phase feeding significantly more in females (72%) than males (36%). In both sexes, LPS anorexia was mediated by a decrease in meal frequency without any change in meal size. Because illness anorexia is an important aspect of the APR, these data are further evidence for the importance of sexual differentiation in immune system function. Additionally, because these effects correspond closely to previous results in estradiol-treated ovariectomized rats, it is likely that endogenous estradiol is an important mediator of the increased potency of LPS. Supported by DK 54523.

Mu receptor activation in the parabrachial nucleus (PBN) increases food intake in rabbits. K.J. SIMANSKY, D.M. NICKLOUS, *Dept. Pharmacology & Physiology, MCP Hahnemann University School of Medicine, Philadelphia, PA 19102, USA.*

In rats, stimulating opioid receptors in the lateral PBN with the mu receptor agonist DAMGO increases eating. Rabbits have been useful for studying taste physiology, controls of orofacial musculature and other aspects of ingestion. To further our understanding of the brainstem neurocircuitry relevant for eating in rabbits, we tested the orexigenic action of parabrachial infusion of DAMGO. Four adult male Dutch belted rabbits were implanted bilaterally with stainless steel cannulas to end 1mm above the lateral PBN; injectors extended 1 mm further. They were housed individually and provided with continuous access to standard chow and water, with lights on from 07:00 hr - 19:00 hr. At 10:00 hr, the rabbits were infused bilaterally into the lPBN with either 0 (saline), 0.016, 0.062, 0.25 or 1 nmol DAMGO in 0.5 ul. All doses of DAMGO increased cumulative food intake significantly during the 6-hr test from 16.9 +/- 3.0 g (saline) by 46, 71, 134 and 55% respectively ($p < 0.001$). The hyperphagia had a delayed onset, as in rats, with none of the doses increasing intake during the first 30 min but all doses doing so by 2 hr. In a separate group of 5 rabbits, infusion of 2 nmol/side of melanin concentrating hormone (MCH) failed to alter feeding. These data are consistent with a mu opioid-mediated orexigenic circuit in the PBN of lagomorphs as in rodents and suggest that MCH does not act within that region to increase eating. Supported by MH41987 and DK58669 to KJS.

Gastric emptying and intragastric pressure during and following multiple meals in rhesus monkeys. U. SMEDH, S. KNIPP, T.H. MORAN, *Dept. of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.*

Rates of liquid nutrient gastric emptying are rapid and volume related during the time a meal is consumed or during an intragastric infusion. Following the meal, emptying slows and the rate is determined primarily by the caloric concentration of gastric contents. The present experiments were aimed at determining how emptying rates were affected across multiple meal infusions and how alterations in intragastric pressure may contribute to changes in emptying rates during these periods. Male rhesus monkeys equipped with chronic indwelling gastric cannulas were the experimental subjects. Glucose test meals (0.25 g/ml) were infused at a rate similar to the rate at which monkeys normally would ingest the glucose (25 ml/min). Volumes of 75, 150 or 225 mls were infused at time 0 and again 20 min later. Volumes remaining in the stomach were determined by dye dilution throughout and following the infusions. In response to second meal infusion emptying rate increased transiently. The timing and extent of the increase depended on the relative volumes. Following an initial 75 ml infusion, the emptying rate increase occurred during the subsequent 150 ml infusion. Following an initial 150 ml infusion, the increase in emptying rate in response to the second infusion was delayed. Following an initial 225 ml infusion, the effect of a subsequent 150 ml infusion was less clear. Intragastric pressure data demonstrated relatively greater pressure during than following gastric fill. These pressure increases may account for the relative differences in emptying rate during and following meal infusion. (Supported by DK19302).

Standardizing adjective-labeled scales: Are all maximum intensities the same to all people? D.J. SNYDER, V.B. DUFFY, K. FAST, B.G. GREEN, L.M. BARTOSHUK, *Dept. of Surgery (Otolaryngology), Yale University School of Medicine, New Haven, CT 06520-8041, USA*.

We cannot share each other's experiences. Consequently, sensory or hedonic intensity cannot be compared directly across individuals or groups. However, indirect comparisons are possible using a standard assumed to be equal, on average, to those being compared. While sensory standards have been used successfully (e.g., magnitude matching), we are interested in the use (and misuse) of intensity descriptors as standards (e.g., rating scales). Range theory, developed by Borg and Teghtsoonian, argues that the maximum perceivable intensity is equal for all sensory modalities and individuals. If true, this would allow across-subject comparisons because all judgments could be made on a scale from zero to maximum; this tacitly assumes that the absolute intensities denoted by intensity descriptors are equal to everyone for everything. Our data contradict these assumptions. Using the general Labeled Magnitude Scale (gLMS), which is anchored at the top with "strongest imaginable sensation of any kind," subjects (N=283) rated the perceived intensities of remembered sensations from various modalities, along with the taste of PROP (6-n-propylthiouracil). The intensities of the strongest sensations remembered for each modality were significantly different, implying that maximum perceivable intensity is not equal for all sensory domains. Also, strongest tastes and oral burn were correlated with PROP bitterness, suggesting that the maximum perceivable intensity within a domain varies across individuals. We conclude that scales anchored in terms of a single sensory domain (e.g., VAS) are less likely to produce valid across-subject comparisons than those with anchors outside the domain under study (e.g., gLMS). (DC00283)

Gastrointestinal controls of feeding in a mouse model. J.P. SOKOLNICKI, A.V. AZZARA, G.J. SCHWARTZ, *Dept. Psychiatry, NY-Hospital Weill Cornell Medical College, White Plains, NY 10605, USA.*

To begin to evaluate the role of gut-brain communication in the control of food intake in the mouse, we assessed ingestive behavior and patterns of c-fos expression in the central nervous system in male C57B6J mice in 3 situations: 1) during daytime scheduled 60 min access to a 12.5% glucose solution, 2) following a 1 ml/10 min 12.5% glucose gastric preload, and 3) following i.p. cholecystokinin octapeptide (CCK, 4-10 ug/kg) after 5 h daytime food deprivation. Glucose intake during the scheduled meal ranged from 1.5 - 2.1 ml, and both 4 ug/kg CCK and the gastric glucose preload reduced subsequent glucose intake by 40-50%. Glucose intake, glucose preloads and 4 ug/kg CCK produced similar patterns of c-fos activation in the brainstem, (area postrema (AP), nucleus of the solitary tract (NTS) and parabrachial nucleus) and in the forebrain (central nucleus of the amygdala and lateral paraventricular nucleus (PVN). In contrast, a 10 µg/kg CCK dose, used to evoke a stress response in rats, activated c-fos in more AP/NTS neurons than the 4µg/kg dose, and elicited c-fos expression in the medial PVN, the arcuate nucleus, and the cerebral cortex. Intraperitoneal saline vehicle injections and gastric preloads of physiological saline failed to reduce food intake and did not stimulate c-fos expression. These data:1) demonstrate that the mouse shares important functional and neuroanatomical features of gut-brain communication with the rat and 2) encourage further investigation of the gastrointestinal controls of food intake in genetic mouse models of disordered feeding and energy homeostasis. Supported by DK47208

The role of the melanocortin system and the melanocortin-4 receptor in ring dove (Streptopelia risoria) feeding behavior. A.D. STRADER[1], H.B. SCHIÖTH[2], J.D. BUNTIN[1], [1]*Dept. of Biological Sciences, University of Wisconsin-Milwaukee, Milaukee, Wisconsin. 53211,* [2]*Dept. of Neuroscience, Uppsala University, BMC, Box 593, 751 24 Uppsala, Sweden.*

The melanocortin-4 receptor (MC4-R)is an important mediator of the effects of two melanocortin system ligands, alpha melanocyte stimulating hormone(a-MSH) and agouti-related peptide (AGRP), on feeding behavior and energy balance in mammals. Although an avian homologue of the mammalian MC4-R has recently been identified, there is little information on the role of this receptor and the melanocortin system in avian feeding and body weight regulation. In these studies, we measured changes in feeding behavior in ring doves (Streptopelia risoria) following intracerebroventricular (i.c.v.) injection of various melanocortin receptor agonists and antagonists. The selective MC4-R antagonist HS014 elevated food intake within 4 h at all three doses tested (0.02, 0.2, 2.0 nmol). A 1 nmol dose of the endogenous antagonist AGRP also stimulated feeding but only after a post-injection interval of 10 h. Suprisingly, the MC3-R and MC4-R antagonist SHU9119 not only failed to stimulate food intake at the same doses as HS014, but actually inhibited food intake at 8 h after injection. Whether this was due to toxicity effects or differences in the pharmacology of avian and mammalian melanocortin receptors remains to be determined. Food deprived doves showed a 4-fold increase in the number of AGRP-immunoreactive cells in the tuberal hypothalamus and 5 ng of the MC3-R and MC4-R agonist MT-II significantly attenuated the amount of food consumed by food deprived birds that were allowed to re-feed. These data support a role for the melanocortin system and the melanocortin-4 receptor in ring dove feeding behavior.

Cannabinoid regulation of appetite in lean and diet-induced obese rats. D.S. STRIBLING, R.E. CAMACHO, K.M. ROSKO, G.J. HICKEY, D.E. MACINTYRE, A.M. STRACK, L.P. SHEARMAN, *Dept. of Pharmacology, Merck Research Laboratories, Rahway, NJ 07065, USA.*

CB1 cannabinoid receptors are present in hypothalamic regions implicated in feeding. Both endocannabinoids and exogenous cannabinoid agonists such as Ä-9-tetrahydrocannabinol stimulate feeding in rodents. We evaluated the effect of the CB1 receptor inverse agonist AM251 on food intake in lean and diet-induced obese (DIO) male rats. Lean (approx. 5% body fat) Charles River Sprague-Dawley (SD) rats were raised on a standard rodent diet (Harlan Teklad, 6% fat). DIO SD rats were placed on a moderate-high fat diet (Research Diets D12266B, 32% fat) at 4 weeks of age and were tested at 12-16 weeks of age (approx. 15-22% body fat). AM251 (0.3, 1, 3, or 10 mg/kg, p.o.) or vehicle was administered 1 hr before dark onset. In DIO rats, AM251 caused a dose-dependent reduction in cumulative food intake. The minimal effective dose of AM251 was 1 mg/kg, eliciting a 28.3% reduction in food intake at 18 hrs. In DIO rats, 3 and 10 mg/kg AM251 elicited 49.5% and 82.1% inhibition of feeding, respectively. AM251 reduced food intake to a lesser extent in lean rats. AM251 at 10 mg/kg in lean rats suppressed overnight food intake by 44.3% while 3 mg/kg caused a 22.6% reduction. Rats made obese through consumption of palatable chow were more sensitive to the anorectic effects of AM251. Differences in body composition (adiposity) or diet between lean and DIO rats may explain the differential sensitivity. These studies provide insight into the importance of CB1 receptors in the control of appetite.

Control of water intake and neurohypophyseal hormone secretion in rats fed high-NaCl diet. E.M. STRICKER, M.L. HOFFMANN, C.A. SMITH, A.F. SVED, *Dept. of Neuroscience, University of Pittsburgh, Pittsburgh, PA 15260, USA.*

Recent experiments indicate that dehydrated rats diminish thirst and neurohypophyseal hormone secretion soon after water consumption begins, which is well before absorption of water has diluted osmolality in systemic blood sufficiently to be detected by cerebral osmoreceptors. Similarly, rats given gastric loads of hypertonic saline increase thirst and neurohypophyseal secretion well before significant increases in systemic plasma osmolality have occurred. These and other findings suggested that visceral osmoreceptors (or Na+-receptors) play an important role in the control of body fluid homeostasis. In each of the experiments to date, rats had been maintained on standard chow which contains 1% NaCl by weight. The present series of experiments examined these issues in rats that had been maintained instead on food pellets containing 8% NaCl. Rats fed this high-NaCl diet ate normal amounts of food daily but increased their water intake 2-3 fold. The additional water intake is known to be stimulated by the osmotic effects of the NaCl load embedded in the food, but preliminary results indicate a second basis of enlarged drinking bouts: the very high Na+ concentration of fluid present in the stomach in association with partly digested food, which serves to concentrate the fluid that enters the intestines and thus makes ingested water much less effective in rehydrating the animal. Ongoing experiments are exploring changes in vasopressin and oxytocin secretion that occur in these circumstances.

Food intake in the elderly. N. STROEBELE, J.M. DE CASTRO, *Georgia State University, Atlanta, GA 30303, USA.*

External factors such as presence of other people, location, as well as time of consumption, have a significant impact on food intake. An increase of the number of people present as well as eating in full-service and fast food restaurants tend to increase food intake. This seems to be especially important for the elderly who show reduced overall intake in association with a reduction in social facilitation and restaurant visits. These external factors may influence the state of arousal (mood) during food intake. A diet-diary was used for data collection. The participants were instructed to maintain a detailed diary about their eating habits including their arousal state for 7 consecutive days. Results show significant increases in intake with more people present as well as with full-service and fast food restaurants across all ages. Participant's mood ratings are significantly more positive when eating out in comparison to eating at home and with one or more people present, independent of the time of consumption. All age groups show significant correlations of food intake and arousal state. More elated mood was associated with a higher intake. Arousal could be a mediating factor between social and environmental stimuli and intake. The results show that the elderly appear to be influenced by environmental factors in similar ways and to the same extent as younger individuals. Changes in the social and environmental conditions of eating may be useful to induce positive changes in food intake of the elderly.

Do metabolic signals stimulate intake in rat pups? S.E. SWITHERS, *Dept. of Psychological Sciences, Purdue University, West Lafayette, IN 47907-1364, USA.*

Signals generated by administration of agents that interfere with metabolism of glucose or fats (such as mercaptoacetate [MA] or 2-deoxyglucose) have repeatedly been demonstrated to influence intake in adult rats. In rat pups, demonstrations of the effects of such agents have been less robust. Recent work in our lab has focused on examining the effects of MA and methyl palmoxirate on independent ingestion in pre- and peri-weaning rats. Our results suggest that drugs like MA can produce physiological effects in very young pups, but pups aged 9 days or younger do not respond to these physiological changes with enhanced intake. Pups aged 12 or 15 days show both physiological changes and increased intake following administration of MA. However, the context in which intake is assessed is critical for determining the effects of MA on intake in rat pups, since increased intake is demonstrated in 12- and 15-day-old pups only in a limited set of circumstances. Further, the age at which MA first stimulates intake can be affected by the diet on which the dam has been maintained. Finally, administration of MA to pups older than 15 days of age results in altered physiology, but not increased ingestion. Taken together, the results suggest that the development of behavioral responses to altered fatty acid oxidation in rat pups follows a complex trajectory that is not yet fully understood.

Hypothalamic neuropeptide expression in obese adult cloned mice. K.L.K. TAMASHIRO[1,2], T. WAKAYAMA[3], H. AKUTSU[3], Y. YAMAZAKI[3], J.P. HERMAN[2], S.C. WOODS[2], R. YANAGIMACHI[3], R.R. SAKAI[2], [1]*Neuroscience Program and* [2]*Dept of Psychiatry,* [2]*Univ. of Cincinnati Medical Center,*

Cincinnati, OH 45267, USA and [3]Institute for Biogenesis Research, Univ. of Hawaii School of Medicine, Honolulu, HI 96822, USA.

B6C3F1 mice cloned from adult cumulus cells exhibit adult-onset obesity when compared with age-matched control mice that were derived from normally fertilized embryos that were cultured in vitro and transferred into surrogate mothers. Cloned mice were not hyperphagic as adults but had high levels of plasma insulin and leptin, and appear to have a more sensitive melanocortin signaling system. Interestingly, the obese phenotype was not transmitted to offspring (B6C3F2) when male and female clones were mated. A second strain of female clones, B6D2F1, was also found to be heavier than stock animals at the same age (42.4 ± 3.5 g vs. 30.0 g). In addition, male B6D2F1 mice cloned from fetal neurons are heavier than age-matched control mice (56.5 ± 0.9 g vs. 43.2 ± 1.0 g). These data suggest that higher body weight in cloned mice is not dependent on background strain or donor cell type. Expression of several hypothalamic peptides and receptors involved in body weight regulation was examined, including NPY, AgRP, POMC, and the MC-4 receptor. In addition, IGF-I and IGF-II receptor and ligand mRNA expression in the brain of adult cloned mice of both strains and B6C3F2 offspring was measured. Together these measures may provide further understanding of the long-term effects of obesity in cloned mice. Supported by DK48061 (RRS), MH49698 (JPH), and grants from the Kosasa Family Foundation, Victoria S. and Bradley L. Geist Foundation, and Katherine and Harold Castle Foundation (RY).

PROP taster status and sensory responses to sweetened and unsweetened milk mixtures. B.J. TEPPER, G.L. GOLDSTEIN, N.V. ULLRICH, *Dept. of Food Science, Rutgers University, New Brunswick, NJ 08901, USA.*

Previous studies suggest that genetic taste sensitivity to the bitterness of 6-n-propylthiouracil (PROP) is positively associated with the perception of creaminess in unsweetened dairy products. However, studies with sweetened dairy mixtures have failed to show this effect. It is possible that adding sweetness to dairy mixtures creates "sensory confusion", reducing the PROP effect. The objective of this experiment was to determine if greater responsiveness to PROP was associated with higher perceived creaminess in unsweetened as compared to sweetened dairy mixtures. Seventy-nine, normal-weight, young adults participated. They were classified as PROP non-tasters (n=26), medium tasters (n=30) or super-tasters (n=23) using PROP and NaCl impregnated filter paper disks according to Zhao et al., 2001 (abstract). Subjects rated two sets of samples; unsweetened and sweetened (6% sucrose) milk-oil mixtures prepared with fat-free milk and varying concentrations of vegetable oil (0, 5, 20% w/v). Ratings for sweetness, flavor, creaminess and overall liking were collected using 15-cm line scales. Sweetened samples were rated more sweet, flavorful and creamy than unsweetened samples ($p<0.01$-0.001). Sensory ratings for both sweetened and unsweetened samples increased across concentrations ($p<0.001$), but creaminess ratings rose more rapidly for super-tasters than the other groups ($p<0.01$). Also, at the hedonic peak (5% fat), non-tasters liked the sweetened sample more than super-tasters ($p<0.05$). Contrary to expectations, these data suggest a moderate influence of PROP taster status on perceived creaminess and liking of sweetened milk mixtures. These findings are generally consistent with, but less robust than, previous findings from our laboratory on salad dressings.

The relationship between neuropeptide Y (NPY) and ethanol-related behaviors in mutant mice lacking specific NPY receptor and in rats selectively bred for alcohol preference. T.E. THIELE[1], N.E. BADIA-ELDER[2], *[1]Dept. of Psychology, University of North Carolina, Chapel Hill, NC, 27599-32701†., [2]Dept. of Psychology, Indiana University/Purdue University, Indianapolis, IN 462022, USA.*

Genetically engineered mouse models and selectively-bred rat lines are powerful tools for investigating the roles of genetic, neurochemical and behavior factors related to ethanol drinking. Mice that completely lack NPY consume more ethanol, and are less affected by ethanol-induced intoxication, in comparison to wild-type controls. Conversely, transgenic mice that overexpress NPY drink less ethanol but show increased sensitivity to the ethanol-induced sedation. When mutant mice lacking specific NPY receptors were examined, Y1-receptor knockout mice consumed more ethanol, and were less sensitive to ethanol-induced sedation, than wild-type controls. However, consumption of sucrose or quinine solutions and plasma ethanol levels did not differ. On the other hand, Y2-receptor knockout mice drank less ethanol than wild-type controls, and Y5-receptor knockout mice did not differ from controls. In addition, intracerebroventricular (ICV) administration of NPY reduced ethanol intake in selectively-bred alcohol-preferring (P and HAD) rats, but had little or no effect in alcohol-nonpreferring (NP and LAD) rats. ICV administration of NPY increased ethanol-induced sedation in both P and NP rats. Thus, in agreement with the studies testing NPY mutant and transgenic mice, enhanced NPY activity appears to be associated with low ethanol intake and with increased ethanol-induced sedation. Ongoing studies with the selectively-bred rat lines are aimed at determining the specific anatomical regions involved with these effects. Taken together, these data suggest the ethanol-induced intoxication and consumption of ethanol are

modulated by central NPY signaling. Supported by AA00258 and AA13573 (UNC) and by AA10722, AA12857, AA07611 (IUPUI).

Food restriction enhances orexin-A stimulated food intake in rats. A.J. THORPE, C.M. KOTZ, *Dept. of Neuroscience, University of Minnesota, Minneapolis, MN 55417, USA*

Orexin-A administered centrally elicits feeding, but the feeding response only occurs during the light phase. The feeding response to orexin A exclusively at this time of day may be related to low hunger signaling from other endogenous potentiators of appetite and the metabolic status of the animal. We hypothesized that sensitivity to orexin-A would be masked under restricted diet conditions where hunger signaling is high. To test this, male Sprague-Dawley with lateral hypothalamus (LH) cannulas were placed on a food-restricted diet for one month. Animals were allowed access to chow daily at 1300 h in quantities sufficient to maintain body weight at 90% of baseline. On the test day, animals received 1 nmol orexin-A or artificial cerebrospinal fluid (aCSF) into the LH just prior to ad libitum access to chow at 1300 h. The study was performed in a crossover design with at least 72 h between treatments. Food intake was measured 2 hours post injection. Orexin-A in the LH significantly stimulated feeding ($p<0.05$) as compared to controls (mean food intake: orexin A, 17.9 ± 0.7 g; control, 12.5 ± 0.8 g). Thus orexin A induced an average intake of 5.4 grams above baseline, which is approximately 2-fold greater than the amount above baseline typically consumed in response to LH-injected orexin A. In contrast to our hypothesis, these data indicate that food-restricted rats have an increased sensitivity to orexin A and suggest that metabolic status may be involved in the circadian specificity of orexin A feeding stimulation.

Thirst and Salt Appetite Responses in Aging Rats. R.L. THUNHORST, A.K. JOHNSON, *Dept. of Psychology and Pharmacology and the Cardiovascular Center, University of Iowa, Iowa City, IA 52242-1407, USA.*

Male Brown Norway rats aged 4 mo (young) and 20 mo (old) received a series of experimental challenges to body fluid homeostasis over approximately 3 mo. Water was available for drinking in some tests and both water and 0.3 M NaCl were available in others. The series included 3 episodes of extracellular fluid depletion (i.e., furosemide plus 20-h sodium restriction), 2 tests involving intracellular fluid depletion (i.e., sc hypertonic saline, 2 ml/kg bw of 6% or 12% NaCl), 1 test involving overnight food and fluid restriction, and testing with captopril adulteration of the drinking water (0.1 mg/ml) for several days. Old rats were significantly heavier than young rats throughout testing. Young rats drank more water and saline following sodium deprivation than old rats, both in terms of absolute intakes and for bw-adjusted intakes. Young rats drank nearly twice as much water as old rats in response to sc hypertonic NaCl when intakes were adjusted for bw. Young rats also drank more saline than old rats following overnight food and fluid restiction when intakes were adjusted for bw. In response to captopril adulteration of the drinking water, young rats increased saline intakes when it was available in choice with water, and increased water intakes when water was solely available, both in terms of absolute intakes and bw-adjusted intakes. Old rats had no response to captopril treatment. These results support previous reports that aging rats have diminished thirst and greatly reduced salt appetite responses to regulatory challenges.

The role of proteins and amino acids in energy nutrients homeostasis. D. TOME, *Physiology of Nutrition and Feeding Behavior, Institut National Agronomique Paris-Grignon, 16 rue Claude Bernard, 75341 Paris cedex 05, France.*

The nutritional significance of variation in protein intake (0.6 to 2.5-3.0 g/kg/d in adult) remains questionable. Protein and energy homeostasis is achieved via (i) peripheral protein and energy metabolism, (ii) sensory and metabolic inputs, and (iii) central control of food intake. The main regulators of these processes are nutrients (mainly glucose and amino acids), hormones (mainly insulin) and neural signals (mainly vagus). The acute response to a meal involves a cascade of peripheral processes in which amino acids, glucose and hormones are potent modulators of nutrients oxidation, protein synthesis and breakdown and lipogenesis. Body protein mass is precisely regulated and cannot be easily modified by increasing protein intake and additional amino acids are utilized in energy pathways. Protein food is very likely to begin to suppress hunger while it is still in the digestive tract. Other post-absorptive metabolic effect of amino acids and energy nutrients have also to be taken into account as well as direct central signals associated to amino acids and glucose. The capacities to adapt to different level of protein intake (15-50 % energy) are probably high. The metabolic advantages to utilize more amino acid in energy pathways and the precise mechanisms underlying the satiating effects of proteins remain to be understood.

Brain mechanism of learned preference for an essential amino acid, lysine in rats with lysine deficiency. K. TORII, M. SMRIGA, T. KONDOH, *Ajinomoto Co. Inc., Kawasaki Kanagawa, Japan.*

A risk of deficiency in the essential amino acid, L-Lysine (Lys) exists in developing regions where cereals supply the major proportion of energy, and also among the elderly in developed countries. Little is known about the physiological consequences of such a deficiency. Rats respond to a Lys-deficient diet with anorexia and an increase in taste preferences for a previously aversive Lys solution. These responses are initiated by endogenous factors, including plasma Lys, activin A and the plastically-activated vagal Lys sensors and the neurons of the nucleus solitarus and the basal hypothalamus. The information reaches the brain and triggers a rapid recovery from the deficiency, as shown by functional MRI and electrophysiological measurements. Plus, microdialysis experiments documented that the ventromedial hypothalamic norepinephine release is specifically involved in the early integration of signals on Lys deficiency. The brain mechanisms of adaptation to Lys deficiency have strong implications for further human studies of Lys fortification.

Mercaptoacetate suppresses intake of a fat-associated flavor in the presence, but not in the absence, of fat calories. A.L. TRACY, T.L. DAVIDSON, *Dept. of Psychological Sciences, Purdue University, West Lafayette, IN 47907, USA.*

It has been demonstrated that the fatty acid oxidation inhibitor Na-2-mercaptoactate (MA) produces a selective increase in appetitive responding for fat-predicting conditioned stimuli in the absence of fat delivery (Davidson, Altizer, Benoit, Walls, & Powley, 1997). Other studies (Singer, York, & Bray, 1998; Ritter, Ritter, & Cromer, 1999) have shown a decrease in fat consumption following MA treatment in macronutrient intake tests. The current study examined this difference in appetitive and consummatory responses to fat induced by MA using a within-compound learning design to train animals to associate particular flavors with the consumption of fat and carbohydrate calories. The animals were then tested for the consumption of the flavors after MA or saline administration in the presence or absence of calories. The MA-induced selective suppression of fat in animals receiving caloric solutions in the test phase was replicated using this design. However, no selective intake effect was seen in MA-treated animals tested with non-caloric solutions. These results suggest that the effects of MA on consummatory behavior directed towards fats and fat-associated stimuli are dependent on the postingestive effects of consuming fat calories and that these postingestive effects are a necessary element in the selective MA-induced suppression of fat intake.

Anorexia Nervosa: A neurodevelopment disorder. J. TREASURE , F. CONNAN, S. LIGHTMAN, I. CAMPBELL, *Department of Psychiatry, Guys Campus, The University of London, London SE1 9RT, UK.*

Anorexia nervosa (AN) is a disorder of complex aetiology. Genetic, biological, psychological and sociocultural factors each appear to make a significant contribution to the susceptibility to AN. However, few of these risk factors are specific to the disorder and no single factor is either necessary or sufficient to generate disorder. A multifactorial threshold model, emphasising gene-environment interaction, is therefore an appropriate explanatory model. It is hypothesised that genetic factors and early life experience interact to generate susceptibility to a dysregulated stress response. Psychosocial and biological changes associated with puberty exacerbate this vulnerability, such that when it is encountered maladaptive coping (inter and intra personal submission & defeat) transforms it into strain with an aberrant HPA axis response. Specifically, the HPA axis fails to adapt to the chronicity of a stressor, in that there is persistently elevated corticotrophin releasing hormone (CRH) activity rather than a switch to an alternative ACTH secretagogue. The continued elevation of CRH release causes the loss of appetite to persist with the loss of nutritional homeostasis. Data from both the basic sciences and clinical research will be presented to support this neurodevelopmental model for the aetiology of AN.

Molecular and physiological changes in trigeminal neurons precede the onset of chewing in rats. J.E. TURMAN, Jr.[1], S.H. CHANDLER[2], [1]*Dept. of Biokinesiology and Physical Therapy, University of Southern California ,*[2]*Dept. of Physiological Science, University of California, Los Angeles, CA 90089, USA.*

The development of ingestive behaviors includes a transition from sucking to chewing. We hypothesize that plasticity in brainstem oral-motor circuits contributes to this transition. To test this hypothesis, we examined developmental changes in molecular and functional properties of trigeminal motoneurons (Mo5) and mesencephalic trigeminal neurons (Me5). One characteristic associated with rhythmical movements, such as

sucking and chewing, is neuronal bursting. We previously showed that NMDA receptor activation contributes to burst generation in Mo5. Furthermore, others have shown that slow inward rectifying currents (Ih) sculpt neuronal bursting patterns. This study examined the developmental expression of NMDA receptor subunits and hyperpolarization-activated cation channels (HCN), which generate Ih currents, in postnatal day (P) 0-21 rats. NMDA subunit, HCN2 and HCN4 expression was detected using immunohistochemistry and/or RT-PCR. Whole-cell patch clamp recordings from in vitro brainstem slices were obtained to analyze physiological changes. Physiological data reveal the emergence of Mo5 NMDA-induced bursting at P8-12, which is coincident with neuroanatomical data showing significant changes in the ratio of Mo5 NMDA receptor subunits. Physiological data also revealed a developmental regulation of Ih currents in Me5 neurons. The strong Ih current observed between P10-12 was accompanied by an increase in HCN2 and HCN4 protein expression. Our data demonstrate a developmental regulation of NMDA subunits and HCN proteins in Mo5 and Me5. In both nuclei, significant changes occur between P8-12, the time period immediately preceding the onset of immature chewing. Our findings suggest synaptic and intrinsic membrane plasticity among trigeminal neurons contributes to the sucking to chewing transition.

Avoidance of a gustatory CS and subsequent cocaine self-administration depend upon the nature of the CS. R.C. TWINING, V. SANCHEZ, K. WARDROP, P.S. GRIGSON, *The Pennsylvania State College of Medicine, Hershey, PA 17033, USA.*

We have hypothesized that rats avoid intake of a saccharin cue when it is paired with a drug of abuse because they are anticipating the rewarding, rather than the aversive, properties of the drug (Grigson, 1997). In support, avoidance of the saccharin cue following taste-i.v. cocaine self-administration pairings is associated with an increase in instrumental responding for the drug of abuse rather than a decrease, as is seen with LiCl-induced conditioned taste aversions (CTAs, White, et al., 1977; Grigson and Twining, 2002). In the current investigation, this association was maintained whether rats had 5 min access to a palatable 0.15% saccharin CS or to more aversive gustatory CSs (e.g., 0.01 M malic acid or 0.0003 M quinine hydrochloride) prior to cocaine self-administration. Rats that had access to the more aversive gustatory CSs, however, tended to take more cocaine self-infusions than rats that had access to the saccharin CS. In addition, those rats that suppressed their intake of the gustatory CS to the greatest extent (referred to as the large suppressers), not only infused the most cocaine, but also evidenced the highest levels of circulating corticosterone following exposure to the gustatory CS on the final test day. Supported by DA 09815 and DA 12473.

The role of capsaicin sensitive afferent nerves in the control of energy. E.H.E.M. VAN DER WALL, E.R. POMP, D.X. GRAM, A.J.W. SCHEURINK, *Dept. of Neuroendocrinology, University of Groningen, PO Box 14, 9750 AA Haren, The Netherlands.*

The role of capsaicin sensitive nerves in the regulation of glucose homeostasis, satiety and meal-induced thermogenesis was investigated in rats treated neonatally with either capsaicin (CAP) or vehicle (VEH). In the first set of experiments, intravenous glucose tolerance tests (IVGTT, 150, 300 and 450 mg in 30 min) were performed to measure glucose tolerance and insulin sensitivity. The insulin response was reduced in CAP compared to VEH. This points to an increased insulin sensitivity in CAP, because glucose tolerance and baseline levels of glucose and insulin were not different between the groups. In the second set of experiments, the effect of capsaicin treatment on short term satiety was investigated by measuring the intake of different concentrations (10%, 15%, 20%, 40%, 10%) of sucrose solution during 1-h. CAP overconsumed at all concentrations, with the strongest effects at 10% sucrose. It was concluded that in CAP satiety was regulated at a higher, relatively constant level and that both volume and osmolality/caloric factors were involved. VEH regulated exclusively on volume. Meal-induced thermogenic responses were also measured (by radiotelemetry) during these experiments. Results indicated that maximum core temperature was controlled during sucrose intake in both VEH and CAP. However, CAP showed a significantly higher maximum and a larger variation in thermogenic response to sucrose. In summary it can be said that, although CAP are still capable to deal with physiological challenges, they miss a fine tuned regulation, suggesting a role of the capsaicin sensitive nerves for the integration of peripheral signals.

Neonatal endotoxin exposure increases alcohol intake of mice in early adulthood. C.H. VAUGHAN, N.E. ROWLAND. *University of Florida, Department of Psychology, Gainesville, FL 32611-2250, USA.*

Hormonal manipulation during the perinatal period in rodents has been shown to result in permanent effects on brain function. In the present study, we examine whether a physiological stress and attendant activation of the

hypothalamic-pituitary-adrenal axis during early life will affect spontaneous alcohol intake in early adulthood in mice. Hsd:ICR (CD-1) mice were injected intraperitoneally with lipopolysaccharide (LPS) either in the first postnatal week (P3-7) or after weaning (P21-25) to induce acute immunological stress. Two other groups received either saline injections or no injection. Alcohol intake for the four groups was recorded at two intervals, before puberty (P30-44) and after puberty (P50-64). During these intervals, a two-bottle choice between water and beer, either a 5% or 10% concentration, was measured. Before puberty intake of 5% and 10% EtOH was significantly higher for both LPS injected groups than saline injected or non-injected groups. After puberty, both LPS injected groups consumed more 5% EtOH than non-injected mice; there were no significant differences for 10% EtOH intake. The acute anorectic effects of LPS administration were monitored by recording body weights throughout the experiment. Both LPS groups weighed significantly less than the saline and non-injected groups through P38. The group receiving LPS after weaning remained at a significantly lower weight than the non-injected group for the duration of the study. The physiological stress induced by LPS administration during either the first week of life or after weaning was found to reduce body weight gain and to increase preference for alcoholic beer during early adulthood.

Adrenal medulla does not contribute to the compensation of the effects of chronic sympathectomy on feeding. I. VILLANUEVA, L. QUEVEDO-CORONA, R. MARTINEZ-OLIVARES, D. RIVERA, R. RACOTTA, *National School of Biological Sciences, IPN. Mexico City 11340, Mexico.*

Chronic treatment with guanethidine (G) is known to drastically reduce the norepinephrine contents of many peripheral organs. However, G-treated rats do not show parallel alterations in normal physiological functions in which the sympathetic nervous system is known to be involved. Body weight balance, for instance, is barely modified in G-treated rats. Previous results from our laboratory suggest that some adrenergic responses, such as the feeding inhibition induced by exogenous catecholamines, are sensitized under chronic sympathectomy. It is hypothesized that secretory compensation could also occur, since some catecholaminergic tissues resist G insult. In this work, a group of neonate male Wistar rats were submitted to a 3-week long treatment with G in daily 50 mg/kg sc injections. This treatment produced, when adults, a 95% reduction ($p<0.01$) in norepinephrine (NE) contents of both splanchnic and extra-splanchnic organs, but did not affect NE or epinephrine (E) concentration of adrenals and hepatic vagus-associated paraganglia. Adrenal demedullation, which reduces the availability of NE and E, did not alter the inhibitory effect of adrenergic agonists on feeding. These results suggest that some local secretory structures, such as paraganglionic bodies, could constitute a source of catecholamines locally affecting visceral functions independently from circulating catecholamine levels. L. Quevedo-Corona and R. Racotta are fellows of DEDICT-COFAA, IPN. Partially supported by CGPI, IPN, Mexico.

Changes over time in physical activity and effect on body weight. N. VOGELS, G. EGGER, K.R. WESTERTERP, *Dept. of Human Biology, Maastricht University, PO Box 616, 6200 MD Maastricht, The Netherlands.*

The aims of this study were to examine the extent to which changes in physical activity have occurred over time, and whether gains in body weight can be mediated by conscious changes in physical activity. Physical activity levels of four different groups of men (successfully weight-losers or not, historically active and modern-day sedentary workers) were measured and compared, using a tri-axial accelerometer (Tracmor-3). Men who have successfully lost weight, through a specific weightloss program, were active at a level similar to that of men performing activity at a level carried out historically. Both of these groups were in turn significantly more active than modern-day sedentary workers ($p<0.05$) and men who had not been successful at losing weight ($p<0.05$).
Eating behavior had not been affected. A linear regression between weekly average activity levels and the degree of waist loss showed a significant positive association ($r=0.524$, $p<0.05$). These data suggest that a higher activity level facilitates the maintenance of long-term weight loss; this level is likely to approximate activity levels in the past. For the prevention and treatment of obesity an increase in physical activity is necessary, because (long-term) weight loss or weight maintenance is unlikely to occur when people are as sedentary as most people are today.

5-HT1A-receptor activation decreases brain but not peripheral glucose level. J.P. VOIGT, CH. MAYER, A. REX, S. JACOBS, H. FINK, *Institute of Pharmacology and Toxicology, School of Veterinary Medicine, Freie Universität Berlin, 14195 Berlin, Germany.*

The somatodendritic serotonin (5-HT)1A agonist 8-OH-DPAT reduces serotonergic activity in the brain and induces food intake in freely feeding rats. Earlier studies demonstrated also effects of 8-OH-DPAT on peripheral glucose level. The present microdialysis study was aimed to investigate effects of 8-OH-DPAT (300µg/kg) on

lateral hypothalamic glucose in comparison to its effects on peripheral glucose. Food intake leads to an increase in lateral hypothalamic glucose. When 8-OH-DPAT treated rats, however, have no access to food after treatment, a decrease in lateral hypothalamic glucose was observed. This effect is 5-HT1A-receptor mediated. Since the presynaptic effect of 8-OH-DPAT on hypothalamic 5-HT precedes the effect of this compound on glucose in time, one may speculate that the latter effect may be of secondary nature. In contrast, the same dose of 8-OH-DPAT effective in the brain had no effect on peripheral glucose in conscious rats. Only a very high dose of the agonist (1800 µg/kg) had a hyperglycemic effect in the periphery as reported also in previous studies. The present data suggest partly independent mechanisms mediating the effects of 8-OH-DPAT on brain and peripheral glucose, respectively.

Role for CD14 and TLR2 in bacterial product-induced anorexia. C. VON MEYENURG[1], B.H. HRUPKA[1], G.J. SCHWARTZ[2], R. LANDMANN[3], W. LANGHANS[1], [1]*Institute of Animal Sciences, Swiss Federal Institute of Technology, 8603 Schwerzenbach, Switzerland,* [2]*Bourne Laboratory, NY Presbyterian Hospital-Weill Cornell Medical College, White Plains, NY 10605, USA,* [3]*Dept. of Research, University Hospital, 4031 Basel, Switzerland.*

Mice consistently reduce food intake following peripheral injections of bacterial lipopolysaccharide (LPS) and muramyl dipeptide (MDP). Because the cell surface component CD14 and the toll-like receptor 2 (TLR2) have been found to be important in mediating the effects of bacterial products on mammalian cells, we examined the role of these gene products in the anorectic effects of LPS and MDP. In all experiments male CD14-knockout(KO) and TLR2KO mice as well as corresponding wild-type (WT) mice were injected IP at dark onset with LPS (2 mg/mouse), MDP (10 mg/kg), interleukin-1b (IL-1b, 150ng/mouse), or vehicle solution, and food intake was measured at 6, 12, and 24 h. The feeding suppressive effect of LPS was significantly weaker in CD14KO than in CD14WT mice, but was equally potent in TLR2KO and TLR2WT mice. MDP reduced food intake similarly in all WT mice, but its feeding suppressive effect was significantly weaker in CD14KO mice and completely absent in TLR2KO mice. IL-1b reduced food intake similarly in all genotypes tested. These results indicate that CD14 is involved in mediating the anorectic effects of both LPS and MDP, and that TLR2 mediates the feeding suppressive effect of MDP. The data are consistent with the hypothesis that TLR4 rather than TLR2 functions as the true LPS receptor, and that TLR2 is involved in recognition of Gram-positive bacterial products such as muramyl peptides.

Orosensory and postingestive factors in high-fat diet hyperphagia. Z.S. WARWICK, S.J. SYNOWSKI, K.R. BELL, *Dept. Psychology, University of Maryland Baltimore County, Baltimore, MD 21250, USA.*

High-fat (HF) diets typically promote greater intake per day than high-carbohydrate (HC) diets, yet the relative contribution of orosensory and postingestive factors has not been clarified. The postingestive effects of fat alone are sufficient to increase daily intake, as demonstrated in a self-regulated intragastric infusion Paradigm in which intake of HF>HC despite equated taste (Am.J.Phys. 269,R30-7,1995.) When a HC diet is ingested, increased palatability promotes overeating (Am.J.Phys. 270,R1197-1202,1996.) The present study directly assessed the independent and interactive effects of palatability and macronutrient composition on intake and meal patterning in rats. Palatability was manipulated by offering either saccharin (S) or glucose+saccharin (GS); pilot work had verified greater oral intake of GS vs. S. In a between-subjects design utilizing the self-regulated infusion paradigm, rats infused either HF or HC (isocaloric at 2.3 kcal/ml) contingent upon drinking either S or GS. Computerized monitoring of intake recorded the number of "meals" (infusion bouts) consumed per day. Average meal size was calculated by dividing daily intake by the number of meals. Preliminary findings are consistent with the previous observation that HF promotes greater daily kcal intake than HC. This was attributable to the larger meals infused by HF-rats relative to HC-rats. Enhancing palatability increased total daily intake, most notably in HF-rats. Supported by NIH DK55367.

Functional interactions between dehydration and feeding. A.G. WATTS, NIBS-N*euroscience Program, University of Southern, Los Angeles, CA 90089, USA*.

Eating and drinking are motivated behaviors comprised of coordinated sets of neuroendocrine, autonomic, and behavioral motor events. In small mammals they are closely correlated both in their temporal distribution and amounts consumed. We have taken advantage of this relationship in dehydrated animals to investigate the neural substrates of anorexia. Nocturnal food intake is reduced by dehydration by approximately 70%. We propose that the networks that coordinate these events can be divided into three groups: networks that stimulate, those that inhibit, and those that disinhibit ingestive behavioral motor functions. Comparing patterns of forebrain

neuropeptide gene expression following dehydration or paired food restriction using in situ hybridization reveals hunger- and anorexia-specific patterns. Dehydrated anorexic rats also have physiological and neural indicators consistent with starvation, including increased plasma glucocorticoids, reduced plasma leptin and insulin levels, increased neuropeptide Y and decreased pro-opiomelanocortin mRNAs in the arcuate nucleus. These data indicate that during dehydration, despite receiving signals that should increase eating, the neural circuits that stimulate eating are inhibited. We also show that when water is returned, these circuits are very rapidly disinhibited to allow eating. The nature of these networks, which are distributed throughout the brain, will be discussed using neuroanatomical (tract-tracing), endocrine, and behavioral evidence from dehydrated anorexic animals. Emphasis will be placed on the potential role of neuropeptidergic action in the operation of these networks, using the neuropeptidergic innervation of the paraventricular and parabrachial nuclei as examples.

The influence of hormones associated with stress on ingestive behavior. R.S. WEISINGER, J.R. BLAIR-WEST, P. BURNS, D.A. DENTON, M. McBURNIE, M.J. McKINLEY, B. PURCELL, L.L. WALKER J. RIVIER, W. VALE, K. SUNAGAWA, R. SHADE, *Howard Florey Institute, Univ. Melbourne, Vic 3010, Australia, Southwest Foundation for Biomedical Research, TX 78245-0549, USA.*

Experimental stress or peripheral administration of the stress hormone adrenocorticotrophin (ACTH) stimulates Na appetite in several species. The present experiments investigated the influence of corticotropin releasing factor (CRF) or urocortin (UCN) alone, or together with peripheral administration of ACTH, on the ingestive behavior of sheep, mice and baboons. In sheep, CRF, administered into the cerebrospinal fluid (ICV) or UCN, administered ICV or intravenously decreased food, water and Na intakes. Intravenous ACTH increased Na and water intake, but did not alter food intake. Intravenous ACTH-induced increase in Na intake was prevented by UCN. In mice, UCN, administered ICV or peripherally decreased Na intake and transiently decreased food and water intakes. Subcutaneous ACTH-induced Na intake was prevented by UCN. In baboons, ICV CRF or UCN, decreased food intake but did not alter water or Na intakes. Intramuscular ACTH did not increase Na intake at doses that increased cortisol secretion and arterial blood pressure. In conclusion, CRF and UCN decreased food intake in all of the species tested but there were clear differences in the decrements produced. ACTH appeared not play a role in this inhibition of food intake. Also, while ACTH stimulates Na appetite in many nonprimate species, this was not observed in the baboon. In sheep and mice, the failure of UCN to consistently stimulate Na intake, despite its ability to stimulate the secretion of ACTH, suggests that UCN influences mechanisms that inhibit Na intake. Finally, the mechanisms by which both ICV and intravenous UCN cause changes in intake are still to be determined.

Habitual meal frequency differentially related to resting and activity induced energy expenditure in younger and older men. M.S. WESTERTERP-PLANTENGA, A.H.C. GORIS, E.P. MEIJER, K.R. WESTERTERP, *Dept. of Human Biology, University of Maastricht, P.O. Box 616, 6200 MD Maastricht, The Netherlands.*

Previously we showed energy intake regulation being a function of habitual meal frequency, which appeared to be determined by blood glucose patterns, in young men. Here we assessed habitual meal frequency in relation to resting and activity induced energy expenditure (REE; AEE). In 10 older women (BMI: 27.5±6.9 kg/m2), 15 younger women (BMI: 21.9±2.3 kg/m2), 12 older men (BMI: 25.7±3.3 kg/m2), 19 younger men (BMI: 22.9±1.8 kg/m2) habitual meal frequency was determined by doubly labelled water validated food intake diaries, physical activity by tri-axial accelerometers, and REE by a ventilated hood system. No relationship of meal frequency with the parameters assessed was observed in the women. In the older men meal frequency was positively related to REE ($r2=0.4$; $p<0.05$), but not to the residuals of REE as a function of FFM, and inversely related to AEE ($r2=0.3$; $p<0.05$). REE explained 40% of the variation in meal frequency; adding AEE explained 60%. In the younger men, meal frequency was inversely related to REE ($r2=0.8$; $p<0.0001$), to the residuals of REE as a function of FFM ($p=0.03$), and positively to AEE ($r2=0.6$; $p<0.0001$). REE explained 85% of the variation in meal frequency; adding AEE explained 89%. We conclude that in men habitual meal frequency was a function of REE and AEE, but in different directions. Only in young men EI was shown to be a function of meal frequency, so we speculate that in those, meal frequency might be a tool in tuning EI to EE.

Fischer 344 rats are more sensitive to the aversive kappa-mediated effects of opioids than Lewis rats. R.A. WHEELER, C. LIU, K.W. SANCHEZ, N. SUBLETTE, E. LEUENBERGER, P.S. GRIGSON, *Penn State College of Medicine, Hershey, PA 17033, USA.*

Fischer 344 rats exhibit greater avoidance of saccharin when paired with morphine than do reward-preferring Lewis rats. Given evidence suggesting that Fischer rats are more sensitive to k agonists, we hypothesized that

morphine-induced saccharin avoidance is mediated by k receptors in Fischer rats and by m receptors in Lewis rats (mediating aversive and rewarding opioid properties, respectively). We investigated possible strain differences involving m and k opioid receptors in 3 experiments. Experiment 1 confirmed that Fischer rats demonstrated greater avoidance of the saccharin cue when paired with sc or iv morphine injections. Experiment 2 showed that Fischer rats also exhibited greater avoidance of the saccharin cue when paired with spiradoline, an aversive k agonist. Experiment 3 evaluated the role of m receptors. Lewis and Fischer rats were pretreated with naloxone, a m antagonist, or saline and then presented with saccharin-saline or saccharin-morphine pairings. Blockade of m receptors augmented morphine-induced suppression of saccharin intake in the Lewis rats. Unfortunately, Fischer rats exhibited a floor effect, so it is unclear whether their behavior was altered by the pretreatment. The data suggest that: (1) m receptors mediate reinforcing properties of opioids while k receptors mediate aversive properties; (2) These actions are in opposition; (3) Lewis rats appear more sensitive to the m mediated effects of morphine, while Fischer rats are more sensitive to k mediated activity; (4) When k receptors are unopposed in Lewis rats, a conditioned taste aversion to morphine is exhibited. Supported by DA 05932, DA 09815 and DA 12473.

The effects of (-)-hydroxycitric acid (HCA) and grape seed on food intake, body weight and metabolism. P.Y. WIELINGA, J. LOUTER-VD HAAR, M.G. POELMAN, M. ROMEIJN, A.G. NIEUWENHUIZEN, A.J.W. SCHEURINK, *Dept. of Neuroendocrinology, University of Groningen, PO Box 14, 9750 AA Haren, The Netherlands.*

Several plant-derived compounds are used as dietary supplements for influencing hunger and satiety. In most cases the underlying mechanisms are unknown. Grape seed and (-)-hydroxycitric acid (HCA), the active ingredient in the herbal compound Garcinia Cambogia, are potential candidates that may serve as a food supplement for changing food intake and body weight. Both compounds seem to affect fat metabolism. We investigated the effects of HCA and grape seed on food intake, body weight and metabolism in male Wistar rats. In the first set of experiments, HCA or grape seed were intragastrically administered as a single dose (300 and 40 mg/kg respectively), 30 min before the onset of the dark period. Both grape seed and HCA reduced food intake without major changes in metabolism. In the second set of experiments, HCA and grape seed were given as a food additive from birth (15 g HCA per kg chow, 2 g grape seed per kg chow, controls received chow). HCA supplemented rats were significantly lower in body weight until adulthood. Thereafter the difference disappeared, possibly caused by a significant decrease in both fat oxidation and total energy expenditure. Long-term grape seed supplementation increased body weight throughout life. No compensatory effects on energy metabolism were observed. The effects of HCA and grape seed are consistent with the assumed underlying mechanisms for these compounds, i.e. reduced de novo lipogenesis and increased lipolysis, respectively.

Enhancement of fat intake induced by accumbens μ-opioid stimulation is dependent on activation of selected input and output structures. M.J. WILL, E. FRANZBLAU, A.E. KELLEY, *Dept. of Psychiatry, Univ. Wisconsin Sch. Med., Madison, WI, 53719, USA.*

We have previously shown that administration of the μ-opioid agonist D-Ala2,Nme-Phe4,Glyol5-enkephalin (DAMGO) into the nucleus accumbens (ACC) strongly increases intake of highly palatable substances such as sugar and fat. We have also shown that intra-ACC DAMGO increases neural activation of certain areas known to be involved in the regulation of feeding behavior, as measured by the expression of the immediate early gene c-fos. The present study explored whether activation of these areas was necessary to observe the intra-ACC opioid mediated feeding. We used a reversible-lesion approach to determine whether inactivation of these areas with an acute injection of muscimol would prevent the feeding response elicited by intra-ACC DAMGO. Subjects were implanted with two sets of bilateral cannulae, one set aimed at the ACC, and the other set aimed at either the dorsomedial hypothalamus, lateral hypothalamus, ventral tegmental area, nucleus of the solitary tract, or basolateral amygdala. After baseline feeding was established, all subjects were assigned to four possible treatment groups following a within-subjects design. Therefore, fat intake of all subjects was measured on alternative days following either muscimol (5,20 ng) or saline administered into the structure of interest immediately prior to administration of either saline or DAMGO (250 ng) into the ACC. In all groups, intra-ACC DAMGO led to nearly a 300% increase in fat intake, and this was blocked by prior administration of muscimol into all sites, suggesting their involvement in ventral striatal opioid-induced feeding. Supported by NIDA grant DA09311 and F32 DA14751.

Metabolic and endocrine responses to nutrient loading and food deprivation in chronic decerebrate and intact rats. D.L. WILLIAMS, J.M. KAPLAN, D.E. CUMMINGS[1], H.J. GRILL,

Psychology Dept., University of Pennsylvania, Philadelphia, PA 19104, USA; [1]Medicine Dept., University of Washington, VA Puget Sound Health Care System, Seattle, WA, USA.

Here we addressed the widely held view that neural interactions between hypothalamus and caudal brainstem are important for autonomic and endocrine responses to perturbations in energy balance. The effects of nutrient loads and 72 h of food deprivation were examined in neurologically intact vs. chronic decerebrate (CD) rats with high mesencephalic transection. Body weight was measured daily, and blood samples and temperature were taken before and after gavage feedings of food or water. The most salient difference between CD and control rats was a much more pronounced deprivation-related corticosterone increase in CDs. This suggests that neural communication between the forebrain and hindbrain is required for normal control of this response to metabolic challenge, although the source of the unchecked corticosterone response (HPA vs. sympathetic drive) remains to be determined. Perhaps more surprising than the differences between CDs and controls was the range of variables for which the groups' responses were similar, as exemplified by the following. Deprivation-related weight loss was comparable in CDs and controls. Diet-induced thermogenesis resulting from nutrient (but not water) loads was seen in both groups. Baseline circulating ghrelin levels and their decrease after nutrient loading were not affected by decerebration. Food deprivation decreased insulin to the same level in both groups. The largely normal-like profile of the CD response to nutrient loading and food deprivation indicates that many metabolic and endocrine responses do not require neural integration of forebrain and hindbrain activity.

Four years of feeding: Outcomes of an intensive behavior treatment for severe feeding Problems. K. WILLIAMS, M. GARLAND, K. RIEGEL, *Hershey Medical Center Feeding Program. Hershey, PA 17033, USA*.

Severe feeding problems such as dependence on supplemental tube feedings, significant malnutrition or extreme food selectivity can be resistant to traditional outpatient treatment. Intensive behavioral treatment delivered in a day hospital setting can be an effective and cost efficient method to successfully treat these problems. We examined all children served by the Day Treatment Program for a period of 48 months. Both the outcome at the end of treatment and the cost are reported. Long-term outcomes are also reported. Cost-effectiveness in terms of comparing intensive treatment to the cost of tube feeding is discussed. In addition to reporting the success rate, we also review cases that were not successful and possible reasons for failure, including medical complications and difficulties with treatment adherence. Our conclusion is that an intensive treatment program can be cost effective and produce good results for many children who have severe feeding problems.

The effect of long-term MT-II administration in dietary-induced obesity (DIO) and weight-reduced rats. K. WILMER[1], R.J. SEELEY[1], M.B. JONES[2], R.J. SHELDON[2],[1]*University of Cincinnati, Dept. of Psychiatry, Cincinnati, OH 45220, USA and [2]Procter & Gamble Pharmaceuticals, Mason, OH 45040, USA.*

Subcutaneous administration of melanocortin 3 and 4 receptor (MC3-/4-R) agonists, such as MT-II, produces a reduction in food intake and body weight. The purpose of this experiment was to compare the efficacy of MT-II to alter food intake in rats given either ad lib access to a palatable, high-fat diet or weight-reduced by restricted access to the diet. For this experiment 36 male Wistar rats were fed a 45% high fat diet for 6 weeks. One week prior to MT-II administration the rats were divided into two weight-matched groups. One group remained on the diet ad lib while a second group received a daily allotment that was only 40% of the ad lib groups intake. On the seventh day, half of the animals in each group received osmotic minipumps containing MT-II delivered at a dose of 1mg/kg/day, and the others received pumps containing vehicle (25% PEG-400/saline). All rats then went back to ad lib food access. Even with an initial increase, due to the return to ad lib access, MT-II suppressed food intake in the restricted group resulting in similar food intakes for days 1-6 of both groups receiving MT-II. A significant % change in body weight was found between both MT-II groups and their corresponding vehicle groups. Both MT-II groups ended up at a similar body weight regardless of the difference in their starting body weight. These findings suggest that MT-II is driving the level of body fat in these animals.

CCK-A receptor mediated control of alcohol ingestion in Sardinian alcohol-preferring rats. A. WOLFE, J. SHEAHAN, M. MANGIARACINA, M. MASSI[1], N. GEARY. *Bourne Laboratory, NY Presbyterian Hospital-Weill, Cornell Medical College, White Plains, NY 10605, USA, [1]Dept. of Pharmacological Sciences and Experimental Medicine, University of Camerino, 62032 Camerino, Italy.*

Sardinian alcohol-preferring (sP) rats are a Wistar substrain selectively bred for high spontaneous alcohol intake (ad libitum 10% ethanol:water intake ratio > 3; Colombo, Alcohol Alcoholism 32:443, 1997). Because alcohol (ethanol) is a potent CCK secretogogue (Liddle et al., Gastroenterol. 87:542, 1984), we investigated the effects of CCK-8 and of the CCK-A receptor antagonist devazepide on 10% ethanol intake in sP rats. Rats had free access to food, water, and alcohol except for two weekly 60-min tests that followed 22h alcohol deprivation. Intraperitoneal injections of 0.5-4 µg/kg CCK-8 just prior to alcohol access had significant, dose-related inhibitory effects on 30-min alcohol intake (27-53%). Devazepide (1 mg/kg 30 min prior to CCK injection and alcohol access) significantly reduced the inhibitory effect of 4 µg/kg CCK-8 on alcohol intake. Finally, devazepide alone increased alcohol intake significantly, by about 27%. These data indicate (1) that exogenous CCK inhibits spontaneous alcohol ingestion, (2) that this effect is mediated by CCK-A receptors, and (3) that endogenous CCK acting on CCK-A receptors plays a role in the control of alcohol ingestion in sP rats. This is the first evidence that endogenous CCK is part of the control of alcohol intake in rats that spontaneously ingest pharmacologically relevant amounts of alcohol. Supported by AA12880.

Central administration of the fatty acid synthase (FAS) inhibitor C75 reveals a role for central nervous system (CNS) metabolism in the regulation of energy balance. M.D. WORTMAN, D.J. CLEGG, S.C. WOODS, R.J. SEELEY, *Dept. of Psychiatry, University of Cincinnati College of Medicine, Cincinnati, Ohio 45267, USA.*

Central or peripheral administration of the FAS inhibitor C75 reduces food intake and body weight in rodents. We and others have reported that the CNS is a critical site of action. Despite being anorexic, C75 administration in lean mice leads to a hypothalamic neuropeptide profile similar to the fed state (elevated POMC/CART, decreased NPY/AgRP) suggesting a specific influence on hypothalamic regulatory pathways. Of interest is that obese animals and animals on a high fat diet are sensitive to the effects of C75 suggesting its actions are upstream of systems like leptin and insulin that can become desensitized in obesity. We hypothesized that carbohydrate utilization, rather than fatty acid oxidation, is important for C75's effects. To test this hypothesis we placed animals on a high-fat ketogenic diet and, after confirming they were ketotic, tested the efficacy of C75 to reduce food intake and body weight. Consistent with our hypothesis, there was no difference between C75 and vehicle in ketotic animals. To confirm metabolic state, and not diet content, was responsible for C75 resistance, we allowed each animal to consume either a sucrose or saccharin solution in addition to the ketogenic diet. C75 sensitivity was completely restored in animals that received the sucrose solution while animals that received the saccharin solution remained insensitive. These results suggest that C75's effect is mediated by carbohydrate utilization in brain and that some aspect of glycolysis or glucose oxidation is capable of influencing endogenous energy sensing mechanisms.

How do palatability and satiation interact? M.R. YEOMANS, R.W. GRAY, L. WEINBERG, *Experimental Psychology, University of Sussex, Brigthon, BN1 9QG, UK.*

Palatability is a well known short-term determinant of food intake in humans, and recent data suggest that increasing the palatability of a test meal reduces the degree to which cues associated with prior energy consumption can modify intake. Thus, palatability and satiation appear to interact. What is less clear is how the immediate satiating effects of a food interact with palatability to determine meal size. Here we report two simple experiments which address this issue. Firstly, we contrasted the microstructure of eating at lunchtime for subjects eating two pasta meals, one with a less palatable more energy dense (cheese) sauce, and one with a more palatable but less energy dense (tomato) sauce. As expected, subjects consumed more in the latter condition both in mass and energy. Analysis of changes in appetite within each meal suggested that only with the palatable food did rated hunger increase in the early stages of the meal, and additionally the rate of satiation was slower in this condition. Since this study failed to control for sensory differences, a more controlled follow-up study used a similar technique to analyse consumption of porridge at breakfast, with the test food varying in both palatability (high and low) and energy content (high and low). The effects of palatability were now more evident at high energy density, and overall intake was greater (both as mass and energy) in the high energy conditions. These results are discussed in terms of interactions between learned, sensory and post-ingestive cues in short-term appetite control.

Mixture suppression in nontasters, medium tasters and supertasters of PROP (6-n-propylthiouracil). J. YIEE, V.B. DUFFY, L.M. BARTOSHUK, *School of Allied Health, University of Connecticut, Storrs, CT 06269-2101, USA.*

Subjects (N=65) rated the tastes of 0.32 M NaCl, 1 M sucrose, 0.014 M citric acid, 0.00024 M quinine hydrochloride, all six possible mixtures of two, all four possible mixtures of three and the single mixture of all stimuli. They also rated the taste qualities of foods/beverages (coffee sweetened with sucrose, tonic water, lemonade, grapefruit juice, soy sauce). Bitterness of PROP was rated at the end of the experiment. Subjects used the general Labeled Magnitude Scale (gLMS), which is the LMS developed by Green et al, 1993 with "strongest imaginable sensation of any kind" at the top. By labeling the scale in terms of all sensations, it provides valid across-group comparisons among nontasters, medium tasters and supertasters of PROP. Intensities of the unmixed stimuli correlated with PROP bitterness (as did the total intensities of the foods/beverages). As the number of components increased, the perceived intensity of the components tended to be suppressed but this varied by PROP status. Supertasters perceived the greatest intensities for the unmixed components but this tended to diminish as the number of components increased. For example, unmixed quinine was more than twice as bitter to supertasters than to nontasters but the bitterness of three and four component mixtures was equal to all. Coffee provides a practical example. Black coffee is more bitter to supertasters than to nontasters. Adding at least 10% sucrose makes the bitterness equal to both groups. This suggests that supertasters may ameliorate the bitterness of foods/beverages by adding other tastes.

Odor-cued fasting-anticipatory satiety is influenced by gender and dietary macronutrients. Y. YIIN, L. THIBAULT. *School of Dietetics and Human Nutrition, Macdonald Campus of McGill University, Montréal, Canada.*

Animals can associate orosensory characteristics from food with postingestive effects and adjust meal size to prevent energy deficit. This process involves memory and administration of glucose was shown to have beneficial effects on memory in animals and humans. Therefore two studies using odor-fasting duration conditioning were conducted. In the first study, male and female adult Sprague-Dawley rats were given 1.5 hours to ingest a casein-based test-meal odorized by either vanilla or chicken flavor prior to a 4-hour short-fast or a 12-hour long-fast. Animals went through the training phase with a pseudo-random sequence of six duplicates of each odor-fasting pairing over 4 experimental days, followed by an odor preference test. Only female rats were capable to adjust meal size according to the post-prandial fast duration. A second study examined if a sugar-rich meal can improve acquisition of anticipatory satiety through memory enhancement. Female Sprague-Dawley rats were given either a sugar-rich or a protein-rich test-meal prior to the post-prandial fasts. Animals were conditioned as described in the first study except for: odors used, post-prandial fasts (shortened to 3 and 10 hours) and training phase (elongated to eleven duplicates and followed by an extinction phase). Both dietary groups have acquired the anticipatory satiety. However sugar-rich group, in contrast to the protein-rich group, demonstrated a delayed learning in meal-size adjustment prior to the short fast. The above studies demonstrate the existence of gender and macronutrient differences in food intake regulation. Acknowledgement: research supported by the National Science and Engineering Research Council of Canada (NSERC).

Changes in uncoupling protein (UCP)-subtype expression in response to altered metabolic status during lactation and development. X.Q. XIAO, B. GRAYSON, P. WILLIAMSON, K.L. GROVE, M.S. SMITH, *Division of Neuroscience, Oregon National Primate Research Center, Oregon Health & Science University, Beaverton, OR 97006, USA.*

UCPs modulate basal metabolic rate by dissipating the mitochondrial proton gradient and, thus, may be a target for the treatment of obesity. Whereas the role of UCP1 in thermogenesis of brown adipose tissue (BAT) is well established, uncertainty reigns as to the function of UCP2 and UCP3. In the present study, a quantitative Real-Time PCR analysis was used to investigate expression of UCPs during several conditions: 1) postnatal development, 2) underfeeding or overfeeding during postnatal development, 3) lactation, a model of hyperphagia and negative energy balance due to milk production, and 4) 48 h fasting. In BAT, UCP1 mRNA levels at postnatal day 11(P11) and P16 were low compared with P21 and adult levels. Chronic underfeeding significantly increased UCP1 expression at P11 but decreased it at later ages. Chronic overfeeding significantly upregulated UCP1 expression at all ages tested. Lactation and 48h of fasting remarkedly inhibited UCP1 expression in BAT. In white adipose tissue (WAT), both lactation and fasting significantly upregulated UCP2 expression. In skeletal muscle, UCP3 expression was not changed during lactation but was increased during fasting. Further investigation will determine the changes of UCP2 and UCP3 in WAT and skeletal muscle in response to chronic underfeeding or overfeeding during the postnatal development. These results suggest that the regulation of the expression of UCPs in BAT, WAT and skeletal muscle during lactation is similar to both fasting and obesity. Furthermore, changes in expression of UCPs during development in response to an abnormal diet may underlie the long-term effects on metabolism.

CART-expressing vagal primary afferent neurons: Quantitative assessment of gastrointestinal and medullary projections. H. ZHENG, H.-R. BERTHOUD, *Neurobiology of Nutrition Laboratory, Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, LA 70808, USA.*

Cocaine- and amphetamine-regulated transcript (CART) is expressed in a subset of primary afferent vagal neurons in the nodose ganglia, and has been hypothesized to play a role in the mediation of gastrointestinal satiation (Broberger C, Hokfelt T, Physiol Behav 74, 2001). To determine the peripheral projections of vagal afferent CART neurons we injected the retrograde tracer Fluorogold (2% in saline, 1 microliter/site) into the ventral wall of the stomach (10 equally spaced injections) or duodenum (6 injections) of 3 rats each. Analysis of left nodose ganglion sections immunohistochemically stained for CART and containing the retrograde Fluorogold label showed that 45+3% of all neurons expressed CART with varying intensity from very weak to strong, and that 17+2% of stomach-projecting and 41+3% of duodenum-projecting neurons expressed CART (double-labeled). In another set of 6 rats, unilateral supranodose vagotomy was used to assess the contribution and distribution of vagal afferent CART neurons to the CART fiber plexus in the dorsal vagal complex. Central terminals of vagal CART neurons contributed more than 30% to the CART plexus within the commissural NTS and lateral area postrema, and 15-20% in the medial subnucleus of the NTS and the dorsal motor nucleus. These findings are consistent with a role for CART in the mediation of intestinal satiety. However, lack of effect on food intake of direct microinjections of CART into the NTS (Zheng et al., Soc Neurosci. Abstr. 27, 2001) suggests additional functional roles. Supported by NIH DK 47348.

Erratum: The following abstract is from a presentation at last year's Annual Meeting of SSIB; it was inadvertantly not published last year.

Is glutamate in the Anterior Piriform Cortex-Lateral Hypothalamus pathway (APC-LH) involved in the anorectic responses to indispensable amino acid deficiency (IAAD)? D.W. GIETZEN, B.G. TRUONG, J.E. BLEVINS, P.S. TEH. *Dept. of Anatomy, Physiology and Cell Biology, School of Veterinary Medicine, Univ. Calif. Davis, Davis, CA 95616, USA.*

Animals fed a diet causing IAAD become hypophagic within 1hr. The brain area that senses IAAD may be in the APC, which projects directly to the LH. This projection may be important in the anorectic responses to IAAD. Aja (1999) showed that single axons from the IAAD sensitive site project directly to the magnocellular cells of the dorsolateral LH (MCLH). Monda et al. (1997) showed increased firing rates in the cells of the LH 1/2hr after injection of threonine into the APC of threonine deficient rats. The primary output cells of the APC are glutamatergic, so we examined the effects of glutamate agonists and antagonists both in the APC and in the LH. In the APC, the NMDA antagonist, AP5 (1.6 ug) caused a 31% increase in IAAD intake that lasted 24 hr, while the AMPA antagonist, NBQX (1.0ug) resulted in a 58% increase at 6 hr that also remained elevated at 43% to 24 hr (Truong, 1999). In contrast in the LH, NMDA had no effect on IAAD intake, but AP5 caused a 30% decrease in IAAD intake. Microdialysis for glutamate in the MCLH suggests that glutamate release in the extracellular spaces around the APC terminals is increased (153% of baseline) at 20 min after IAAD, but also after the corrected control diet. Thus, the glutamate system is clearly implicated in the APC in these responses, but further study of the APC-LH pathway in IAAD feeding is needed. Supported by NIH: NS33347, DK50347, DK35747, DK07355, & USDA: NRI 97-3500-4477 & 2000-1049.