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Appetite 42 (2004) 335–416

Appetite

www.elsevier.com/locate/appet

Abstracts

Society for the Study of Ingestive Behavior: Annual Meeting 2004 20–24 July, University of Cincinnati, Cincinnati, Ohio

Guest Editor: Hans-Rudi Berthoud*

***Masterfoods Keynote Lecture Series*:**
Rudolph Leibel, MD: **Molecular physiology of weight regulation.** ***James O. Hill, PhD:*** **Can we turn the tide on the obesity epidemic?** ***E.T. Rolls, PhD:*** **Brain processes that underlie the palatability of food.** ***Leanne L. Birch, PhD:*** **The development of ingestive behavior during infancy and childhood.**

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

Protein content of the maintenance diet influences flavor preferences conditioned by intragastric protein and carbohydrate in rats. K. ACKROFF, A. SCLAFANI. *Department of Psychology, Brooklyn College of CUNY, Brooklyn, NY 11210 USA.*

Rats adjust their intakes of nutrient sources when the protein content of the maintenance diet is altered. To evaluate the importance of learning in protein selection, chow-fed rats were trained to associate oral intake of noncaloric flavored solutions (CSs) with intragastric (IG) infusions of different nutrients. Female rats were given on separate days a CSc flavor paired with IG carbohydrate (16% maltodextrin), a CScp flavor paired with IG carbohydrate/protein mixture (8% maltodextrin + 8% casein hydrolysate) and a CS − paired with IG water. While still maintained on chow, the rats preferred CSc to CS − (89%), CScp to CS − (91%) and the CSc to the CScp (72%). When switched to protein-free (PF) or complete-protein (CD) semi-synthetic diets and given additional training, the CD rats still preferred CSc to CScp (73%) while the PF rats shifted to a mild CScp preference (60%). When returned to chow again, both groups now preferred the CSc. When all rats were fed the PF diet, the PF group returned to mild CScp preference while the CD group learned to increase their CScp preference only after more one-bottle training. These data show that protein-restricted rats learn to increase their preference for an arbitrary flavor paired with IG protein infusions. The protein-based flavor preferences were relatively mild, suggesting that the reward generated by protein is not very potent under these conditions. Rats orally consuming carbohydrate and carbohydrate + protein diets may shift their preference more rapidly when protein restricted because the oral cues are more distinctive and therefore more readily associated with postingestive stimuli. Supported by NIH Grant DK-31135.

GLP-1 release in obese subjects before and after weight loss and weight maintenance. T.C.M. ADAM, M.S. WESTERTERP-PLANTENGA. *Maastricht University, Maastricht, The Netherlands.*

Aim of the study was to investigate Glucagon-like Peptide 1 (GLP-1) release in response to a standard breakfast after a weight loss period of 6 weeks and a consecutive weight maintenance period of three months. 32 obese subjects participated before [BMI (kg/m^2): 30.1 ± 2.6], after weight loss [BMI (kg/m^2):27.9 ± 2.5] and after weight maintenance (3 months) [BMI (kg/m^2):27.6 ± 2.4] in a test procedure in our department. After a fasting blood sample subjects received water (250 ml) and 15 min later a standard breakfast (1.9 MJ). Blood samples were taken every 30 min relative to water intake for 120 min, in order to determine GLP-1, insulin, glucose and free fatty acids. After weight loss of 7.05 ± 3.45 kg, % regain (mean ± SEM) during the weight maintenance (WM) period was 13.32 ± 9.8% (n.s.). Area under the curve (average 0–120) for GLP-1 release was decreased from before compared to after weight loss ($F_{1,31} = 5.22$; $P = 0.03$) and reversed completely during weight maintenance ($F_{1,31} = 20.0$; $P = 0.01$). During weight loss GLP-1 release decreased. During WM, GLP-1 release increased to a level similar to before weight loss. These data suggest, that the temporary decrease in GLP-1 release after weight loss in modestly obese subjects might be an effect of an acute negative energy balance.

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doi:10.1016/j.appet.2004.04.003

Effect of weight loss on GLP-1 release in modestly obese subjects. T.C.M. ADAM, M.S. WESTERTERP-PLANTENGA. *Maastricht University, Maastricht, The Netherlands.*

To assess whether weight loss improves glucagon-like peptide 1 (GLP-1) release in response to a standard breakfast in modestly obese subjects, 32 obese subjects participated in a repeated measurement design before [BMI (kg/m^2): 30.1 ± 2.6; waist (cm): 94.9; hip (cm): 109.3 ± 7.4] and after a weight loss [BMI (kg/m^2):27.9 ± 2.5; waist (cm): 87.3 ± 9.1; hip (cm): 101 ± 8.4] period of 6 weeks. During weight loss subjects received Optifast® in order to replace 3 meals/day. Subjects came to the laboratory and after a fasting blood sample subjects received water (250 ml) and 15 min later a standard breakfast (1.9 MJ). Postprandially, blood samples were taken every half hour relative to water intake for 120 min, in order to determine GLP-1, insulin, glucose and free fatty acids. Appetite ratings were obtained with visual analogue scales. After weight loss baseline GLP-1 was not different compared to before weight loss. Postprandial ?-GLP-1 was significantly lower at 60 min ($F_{1,31} = 10.97$; $P = 0.002$) compared to before weight loss. Area under the curve (0–120) for GLP-1 release after weight loss was significantly lower as well ($F_{1,31} = 5.22$; $P = 0.03$). Ratings of satiety were increased after weight loss at 120 min ($F_{1,22} = 5$; $P = 0.03$) and ratings of hunger were decreased after weight loss at 90 ($F_{1,21} = 4.52$; $P = 0.04$) and 120 min ($F_{1,22} = 4.64$; $P = 0.04$). In modestly obese subjects weight loss decreased GLP-1 response compared to before weight loss.

GLP-1 release and satiety after a nutrient challenge in normal-weight and modestly obese subjects. T.C.M. ADAM, M.S. WESTERTERP-PLANTENGA. *Maastricht University, Maastricht, The Netherlands.*

Previous studies have shown that postprandial GLP-1 release is attenuated in obese subjects compared to the normal-weight. That might be cause for or consequence of obesity. Aim of the present study was to assess whether Glucagon-like peptide (GLP)-1 release after a standard nutrient challenge (breakfast) in combination with or without a galactose/guar gum stimulation is different in normal-weight subjects compared to modestly obese subjects and the accompanying appetite profile. Therefore 28 obese [BMI (kg/m^2): 30.3 ± 2.7] and 30 normal-weight [BMI (kg/m^2): 22.8 ± 1] subjects received a preload of either galactose (50 g)/guar gum (2.5 g)(GG), dissolved in 250 ml water, or water (W) followed by a standard breakfast 15 min later. After a fasting sample, blood samples were taken every 30 min after preload or water for 120 min, to determine GLP-1, insulin, glucose and free fatty acids. Appetite profile was obtained with visual analogue scales. GLP-1 concentrations were increased in the normal-weight (28%) and in the obese (76%) in the GG condition compared to W ($P < 0.05$). Normal-weight subjects had significantly higher GLP-1 concentrations in the W condition compared to obese subjects ($P = 0.03$), but not after GG. Satiety was significantly increased in normal-weight subjects compared to the obese in the GG condition at 30 and 60 min ($P < 0.05$). GLP-1 release in obese subjects was lower than in the normal-weight, but not with a stronger (GG) stimulation. This was not reflected by subjective feelings of satiety. We conclude that disturbed perception of appropriate physiological feedback might contribute to obesity.

Glycemic load, appetite and food intake in humans. R.C.G. ALFENAS, R.D. MATTES. *Purdue University, W. Lafayette, IN 47907-2059.*

Diets comprised of high glycemic load (GL) foods are reported to enhance appetite and promote positive energy balance. The purported augmentation of appetite is attributed to an especially sharp early post-prandial rise of blood glucose followed by a marked release of insulin and subsequent rebound relative hypoglycemia. Support for this hypothesis stems largely from acute feeding trials and longer-term studies lacking control over the macronutrient composition, palatability and rheology of test foods. This study evaluated the effects of consuming high and low GL foods, matched on these properties, on plasma glucose and insulin, appetite and food intake. Following confirmation of the glycemic response (GR) to each of 48 test foods in a pilot study, 39 healthy adults consumed only those eliciting low or high GR ad libitum in the laboratory for 8 days. Glucose and insulin concentrations were determined before and for 2 h following breakfast and lunch on days 1 and 8. Appetite and energy intake were tracked over the entire day. There were no significant differences in plasma glucose or insulin between treatments. Appetitive ratings and food intake were also comparable in participants consuming foods that elicited only a low or high GR in the pilot study. These data indicate that the differential GR to foods tested in isolation under fixed time constraints are not preserved under conditions of chronic, ad libitum consumption of mixed meals.

Beyond the mere observation of weight gain: What next? D.B. ALLISON. *Department of Biostatistics, The University of Alabama at Birmingham, Birmingham, AL, USA.*

Dr Allison will provide an overview of what is currently known about antipsychotic induced weight gain, what some of the key unanswered questions are, and where preliminary evidence suggests we might look for the answers. Since the earliest introduction of antipsychotic medication, it has been noted that its use is frequently associated with unintended and unwanted weight gain. Recently, investigation of this side effect has risen in importance. As newer antipsychotic medications have been produced, other side effects such as extra-pyramidal symptoms and tardive dyskinesia have been reduced, and the side effect of weight gain has therefore become more salient. Additionally, the newer antipsychotic agents, though believed to be of greater therapeutic benefit, tend to produce more weight gain than did the older, conventional agents. In this talk, data on the magnitude of antipsychotic induced weight gain and how it varies across time and drug will be presented. This will be followed by a presentation of epidemiologic data on the prevalence of obesity among people with schizophrenia, and the apparent or predicted consequences of antipsychotic induced weight gain on quality of life, morbidity, and mortality. Subsequently data on treatment of antipsychotic induced weight gain will be presented. Finally, emerging data on mechanisms of action from will be presented.

Moxonidine into the lateral parabrachial nucleus increases meal-associated hypertonic NaCl intake in rats. C.A.F. ANDRADE, S.P. BARBOSA, D.S.A. COLOMBARI, E. COLOMBARI, L.A. DE LUCA JR., J.V. MENANI. *Departamento de Fisiologia e Patologia, Faculdade de Odontologia, UNESP, Araraquara, SP 14801-903, Brazil.*

The activation of the α2-adrenergic receptors by bilateral injections of moxonidine (α2-adrenergic and/or imidazoline agonist) into the lateral parabrachial nucleus (LPBN) strongly increases 1.8% NaCl intake induced by sc treatment with the diuretic furosemide combined with captopril (angiotensin converting enzyme inhibitor). In the present study we investigated the effects of bilateral injections of moxonidine into the LPBN on food deprivation-induced food intake and on meal-associated water and 1.8% NaCl intake. Male Holtzman rats ($n = 14$) with cannulas implanted bilaterally into the LPBN were submitted to 14 h of food deprivation with water and 1.8% NaCl available. Fifteen minutes before the beginning of food, water and 1.8% NaCl intake measurements, the animals received bilateral injections of moxonidine (0.5 nmol/0.2 ml) or vehicle into the LPBN. Moxonidine injections into the LPBN did not change food intake (9.7 ± 0.6 g/120 min vs. vehicle: 9.0 ± 0.8 g/120 min), but increased meal-associated 1.8% NaCl intake (14.9 ± 3.9 ml/120 min, vs. vehicle: 6.1 ± 4.3 ml/120 min), without changing water intake (5.0 ± 1.2 ml/120 min vs. vehicle: 8.2 ± 0.7 ml/120 min). Therefore, moxonidine into the LPBN increases meal-associated 1.8% NaCl intake without changing food or water intake. This increased NaCl intake is consistent with the deactivation of an inhibitory system used to prevent further dehydration, as suggested by our previous works. It is possible that the deactivation is mediated by α2-adrenergic and/or imidazoline receptors within LPBN. Supported byFAPESP,CAPES,CNPq,PRONEX.

Investigation of the development of preferences for flavours paired with caffeine in the real world using interactive technology. K.M. APPLETON[a], K. SAPSEID[a], P.J. ROGERS[a], R. SHEPHERD[b]. [a]*Department of Experimental Psychology, University of Bristol, Bristol, UK;* [b]*Department of Psychology, University of Surrey, Surrey, UK.*

The development of preferences for flavours paired with caffeine has been widely demonstrated in humans in the laboratory. Little work however has aimed to transfer these effects to the real world. This study used a new interactive methodology (The Snackmate) to allow the management of conditioning procedures in the real world. The Snackmate is a Palm Pilot 500 hand-held computer, programmed here to instruct participants to consume two novel flavoured caffeine-containing drinks, one in a low state of alertness and one in a high state of alertness, as determined covertly by previous self-ratings of mood. Eighteen participants undertook five conditioning trials for each drink. The same participants also underwent five conditioning trials for two other novel flavoured caffeine-containing drinks in the laboratory. Liking for all drinks was assessed before and after conditioning. Significant increases in flavour preferences were found in the laboratory (smallest $F(2,34) = 12.02$, $P < 0.01$), but significant effects were not found in the real world (largest $F(2,34) = 2.80$, $P = 0.08$). Significant effects of caffeine on alertness were found in both situations (smallest $F(3,51) = 2.70$, $P < 0.05$). These findings suggest that preferences for flavours paired with caffeine are more difficult to achieve in the real world than in the laboratory. Perhaps an important difference between these situations was that participants had ad lib access to caffeine-containing drinks in the real world but were tested after overnight caffeine withdrawal in the laboratory. These results are then consistent with the possibility that caffeine reinforcement occurs readily following caffeine withdrawal, whereas caffeine's alerting effect is not in itself a strong reinforcer of flavour preference.

Validation of the computerized measurement of appetite and mood using a Palm Pilot 500 hand-held computer. K.M. APPLETON[a], P.J. ROGERS[a], R. SHEPHERD[b]. *[a]Department of Experimental Psychology, University of Bristol, Bristol, UK; [b]Department of Psychology, University of Surrey, Surrey, UK.*

The use of technology in the study of human appetite is increasing. Comparability between tried and tested traditional tools and new technological tools, however, is important. This study investigated the comparability of measures made using 50 mm Visual Analogue Scales on a Palm Pilot 500 hand held computer with traditional 100 mm Visual Analogue Scales completed by paper and pencil. Using a repeated measures design, eighteen people consumed two caffeinated drinks following overnight fasting. Various appetites and moods were measured before and 1 min, 30 min and 60 min after consumption of each drink using paper and pencil measures and computerized measures. No significant differences were found between paper and pencil and computerized measures (largest $F(1,17) = 3.51$, $P = 0.08$). Differences in the effects of the drinks (drink, time and drink by time interaction effects) were found as would be expected considering the experimental procedures used. Greater differences between drinks and over time, however, were found using paper and pencil compared to computerized measures in some scales (smallest $F(3,51) = 3.58$, $P = 0.02$). These findings suggest that computerized measures and traditional paper and pencil measures are comparable tools for data collection, although the computerized measures appear to be more conservative than paper and pencil measures. Advantages of the computer technology lie in its convenience and its potential for use in interactive methodology.

Role of peroxisome proliferator activated receptor β (PPARβ) in lipopolysaccharide(LPS)-induced anorexia. D. ARSENIJEVIC, W. LANGHANS. *Swiss Federal Institute of Technology (ETH) Zurich, 8603 Schwerzenbach, Switzerland.*

To investigate the role of the transcription factor PPARβ in LPS-induced anorexia, we investigated the feeding response to LPS in PPARβ KO mice (obtained from Prof W. Wahli, University of Lausanne) and corresponding WT mice. LPS (4 μg/mouse, IP) reduced 24 h food intake in WT but not in PPARβ KO mice. Also, LPS increased the plasma concentration of tumor necrosis factor α (TNFα) at 90 min after injection in WT but not in PPARβ KO mice. Basal plasma corticosterone was higher and significantly more increased by LPS in PPARβ KO mice than in WT mice. Interestingly, priming with a non-anorectic LPS dose (0.04 μg/mouse) resulted in anorexia to subsequently injected 4 μg LPS in PPARβ KO mice, although the anorexia was attenuated compared to WT mice. No differences between KO and WT mice were seen in feeding responses to LPS after prior LPS tolerance induction. These results demonstrate that PPARβ is required for TNFα production and anorexia in response to peripheral LPS in experimentally naïve mice. Further, priming apparently enables LPS to recruit mechanisms of cytokine production and/or cytokines independent of PPARβ. These mechanisms and cytokines are sufficient to reduce food intake in PPARβ KO mice.

Estradiol-induced increase in satiation after intraduodenal Intralipid involves phosphorylation of CREB in the NTS. L. ASARIAN, N. GEARY. *Bourne Laboratory, NY Presbyterian Hospital–Weill Cornell Medical College, White Plains, NY 10605.*

Estradiol (E) treatment increases the satiating potency of intraduodenal (ID) infusions of the fat emulsion Intralipid, but not that of ID L-phenylalanine, in ovariectomized rats. Intralipid satiation is mediated by CCK-induced vagal signaling. We previously showed that E's effect on Intralipid satiation is associated with a selective increase in the expression of c-Fos in ER-α expressing cells in the NTS just caudal to the AP. To investigate the intracellular signaling pathways that might mediate this effect, we investigated the phosphorylation of the transcriptional regulator cAMP-response element-binding protein (CREB) in these NTS cells. Ovariectomized Long-Evans rats that were cyclically treated with E benzoate received ID infusions of Intralipid or L-phenylalanine 2 d following E. Ninety minutes later their caudal NTS was taken for immunocytochemical detection of either phosphorylated CREB (pCREB) and c-Fos or pCREB and ER-α. Following ID Intralipid, the majority of cNTS cells that expressed c-Fos also expressed pCREB, whereas following ID L-phenylalanine, pCREB was expressed in few or no c-Fos positive cells. Furhermore, almost all cells that expressed pCREB following ID Intralipid were ER-α expressing cells. These data suggest that estradiol acts via ER-α on cNTS cells to increase the responsivity of a pCREB signaling pathway that is sensitive to feeding-inhibitory vagal signals elicited by the presence of fat in the duodenum. DK 54537 (NG).

Estradiol-induced increase in satiation after intraduodenal Intralipid does not increase c-Fos expression in catecholaminergic cells in the NTS. L. ASARIAN, N. GEARY. *Bourne Laboratory, NY Presbyterian Hospital–Weill Cornell Medical College, White Plains, NY 10605.*

Estradiol (E) treatment increases the satiating potency of intraduodenal (ID) infusions of the fat emulsion Intralipid, but not that of ID L-phenylalanine, in ovariectomized rats. Intralipid satiation is mediated by CCK-induced vagal signaling. We previously showed that E's effect on Intralipid satiation is associated with a selective increase in the expression of c-Fos in cells in the NTS just caudal to the AP. Here we report an initial investigation the neurochemical phenotype of these cells. Ovariectomized Long-Evans rats that were cyclically treated with E benzoate received ID infusions of Intralipid or L-phenylalanine 2 d following E. Ninety minutes later the caudal NTS (cNTS) was taken for immunocytochemical detection of c-Fos and of tyrosine hydroxylase (TH), a marker of catecholaminergic cells. ID Intralipid and L-phenylalanine each induced c-Fos in the cNTS. Following L-phenylalanine, about 15–20% of the cNTS c-Fos-positive cells expressed TH. In contrast, following Intralipid, less than 10% of cNTS c-Fos positive cells expressed TH. This result suggests that the increase in Intralipid-induced satiation produced by E in ovariectomized rats does not involve an increase in the activation of cNTS catecholaminergic neurons. Supported by DK 54537 (NG).

Mechanism(s) underpinning short-term change in the hedonic evaluation of snack foods. E.R. ATTON, M.R. YEOMANS. *Department of Psychology, University of Sussex, Brighton, BN1 9QG, UK.*

Alliesthesia and sensory-specific satiety both potentially explain why snack foods decline in pleasantness when consumed. Physiological usefulness is the fundamental factor in alliesthesia and liking for all snacks rests on this variable. In sensory-specific satiety, orosensory satiation is the instigator and only eaten snacks decline. To determine exactly how and why snack foods change in pleasantness when consumed, these two mechanisms were revisited. Three snacks were developed in low and high energy versions (200 kcal difference), which varied in overall energy content (chocolate > yoghurt > apple). Participants ($n = 54$) consumed high and low energy versions of one snack on different test days and rated the pleasantness of all six snacks before and immediately, 30 and 60 min post-consumption. Energy had minimal impact on post-consumption pleasantness, except in the apple condition where the low-energy version contained few calories (40 kcal). In line with sensory-specific satiety, the eaten snack declined in pleasantness relative to the uneaten alternatives in all three cases and maximal change was evident immediately after eating. These results suggest that hedonic change accompanying ingestion is primarily due to sensory-specific satiety, but an effect of energy can not be discounted without further research, as a low threshold may exist above which any energy intake/density effects pleasantness similarly.

Hypothalamic orexigenic peptides stimulate food intake by increasing meal size. A.V. AZZARA, C. FORLENZA, G.J. SCHWARTZ. *Department of Psychiatry, Bourne Laboratory, WMC Cornell University, 21 Bloomingdale Road, White Plains, NY 10605, USA.*

Central melanocortin (MC) 4 receptor signaling has been implicated in the control of food intake and energy homeostasis in humans and rodent models. We have previously shown that central administration of the MC 3/4R agonist MTII in rats reduces food intake by a specific reduction in meal size without a change in meal frequency. These data suggest that central MC4R signaling modulates the controls of meal size. To pursue this suggestion, we evaluated meal patterns and food intake for 4 days in male Sprague Dawley rats following daytime third intracerebroventricular (3icv) administration of the arcuate hypothalamic orexigenic agouti related peptide (AGRP), an endogenous antagonist of the MC3/4 receptor. We also assessed meal patterns during the first four 4 and 24 h after 3icv daytime injections of Neuropeptide Y (NPY) and the NPY receptor agonist peptide YY (PYY), because NPY is colocalized in arcuate hypothalamic nuclei, stimulates feeding, and may share neuroanatomical targets important for AGRP's effects on food intake. AGRP increased food intake, and this increase was attributable to an increase in nocturnal meal size without changing meal frequency. NPY increased food intake and meal size at 4 but not 24 h, with no effect on meal frequency at either time point. In contrast to AGRP and NPY, PYY increased food intake, meal size and meal frequency at 4 h, but these effects were absent at 24 h post-injection. These data: (1) support the idea that central MC4R signaling affects food intake by modulating the controls of meal size, (2) suggest that the neurochemical and neuroanatomical overlap between AGRP and NPY pathways may mediate their similar feeding stimulatory actions, and (3) suggest that PYY acts through distinct effectors to increase meal frequency. Supported by DK47208 and MH65024.

Essential role of ingested energy level vs. food type, for weight loss in obese Zucker rats. B. BECK, S. RICHY. *UHP/EA 3453 Systèmes Neuromodulateurs des Comportements Ingestifs, 54000 Nancy, France.*

Losing weight is a difficult task for obese people as body weight (BW) is not only regulated by feeding and exercising. Environmental factors such as stress can influence energy consumption, utilization and storage. Hedonic factors associated with pleasure and reward can also interfere in these regulations. To ascertain the role of the later, we fed adult obese Zucker rats with a fixed and reduced quantity (48 kcal/d) of either a control (C) diet (16%fat, 64%carbohydrates; d = 4.0) or a high energy (HE) palatable diet (50%fat, 32%carbohydrates; d = 4.9). BW and hormonal changes were measured after 3 weeks of restriction. Both control and HE rats lost about 10% of their initial BW ($P < 0.0001$) without any significant difference between the two diets. Food restriction induced in both groups a significant rise in ghrelin levels ($P < 0.002$) with a tendency to a higher increase in the HE group ($P < 0.10$). It also induced a significant fall in leptin levels ($P < 0.01$) in the control group but not in the HE group. From these results, we can conclude that it is possible to lose weight when eating less but good. Dietary composition had a secondary impact in this short-term weight reduction program. The maintenance of pleasure associated with the meal could help obese people to more strictly follow their regime. Nevertheless, the different variations in hormonal status after restriction indicate that an increased dietary vigilance is necessary when stopping restriction in order to avoid body weight rebound. These data need also to be confirmed in more common types of obesities such as diet-induced obesity.

Male Sprague Dawley rats lack a preference for sucralose solutions. N.T. BELLO#, M.R. BROCKLEY, A. HAJNAL. *Neural and Behavioral Sciences, College of Medicine, Penn State University.*

Sucralose is a non-nutritive chlorinated sucrose derivative. Unlike other artificial sweeteners, this compound is structurally similar to sucrose and is characterized by human subjects as tasting sweet with little or no aftertaste. Despite this, the preference for sucralose in adult male rats has not been investigated. In this study, we used a series of 24 h two-bottle tests to compare sucralose (0.180–0.350 g/l) with either a strongly preferred 0.3 M sucrose or a weakly preferred 0.003 M saccharin solution. We found that rats consumed a small volume of sucralose (~5 ml) and demonstrated a >90% preference for both sweeteners relative to sucralose. Further, we used a wider range of sucralose concentrations (0.1–10 g/l) and compared sucralose with water in a series of 20 min three-bottle tests. Under both water-deprived and water-replete conditions, rats did not reliably prefer any sucralose concentration. An additional series of 20 min three-bottle tests were conducted to determine if the preference for 0.3 M sucrose or 0.003 M saccharin could be affected by the addition of sucralose (0.050 g/l) to each solution. Our results indicated that the mixture of sucrose + sucralose was less preferred to plain sucrose, whereas the mixture saccharin + sucralose had no effect on preference relative to plain saccharin. Overall, these results demonstrate that sucralose solutions or solutions containing sucralose are not preferred by male Sprague Dawley rats at concentrations that humans find sweet. An awareness of the potential species differences in preference for novel sweeteners is critical for basic and applied taste research. Support by NIH grants DC04571 and DC00240.

Central administration of an insulin mimetic reduces food intake in rats on a high-fat diet. S.C. BENOIT, D.J. CLEGG, L.M. BROWN, B.B. ZHANG, S.C. WOODS. *University of Cincinnati, Department of Psychiatry, Cincinnati, OH. Merck Research Laboratories, Rahway, NJ.*

In addition to its many important peripheral functions, insulin acts directly on the brain to regulate food intake and body fat mass. Central administration of insulin reduces food intake and body weight in many species. However, when maintained on a high-fat (HF) diet, animals develop obesity and insulin resistance, major risk factors for type-2 diabetes mellitus. Further, we previously found that maintenance on a HF diet attenuates the anorectic effects of central insulin. Compound 1 (Cpd1) is an insulin mimetic that reduces insulin resistance, adiposity and body weight when administered centrally or orally. In the present studies we compared the effects of central insulin and Cpd1 in rats maintained on either a HF or a matched low-fat (LF) diet. The doses selected (750 ng Cpd1 and 4 mU insulin) reduce food intake comparably in rats maintained on chow. Intra-third ventricular (i3vt) Cpd1 administration decreased 24-h food intake in rats maintained on either the HF or the LF diet (50% and 20% respectively relative to vehicle) ($P < 0.05$). In contrast, i3vt insulin reduced food intake comparably (40% relative to vehicle) to Cpd1 in the LF group ($P < 0.05$) but had no effect on rats in the HF condition. Hence, Cpd1 was efficacious at reducing food intake in insulin-resistant animals on a HF diet. To begin determining the basis of the differences between insulin and Cpd1, a cohort of chow-fed rats was fasted overnight and administered i3vt insulin (4 mU), Cpd1 (750 ng) or vehicle 2 h prior to sacrifice. Using quantitative PCR, insulin, but not Cpd1, reduced hypothalamic AgRP expression by 35% relative to vehicle ($P < 0.05$) while there was no change in NPY expression following either compound. These data suggest that Cpd1 may differentially impact hypothalamic neuropeptide systems that control energy balance and that this may lead to approaches to circumvent insulin resistance.

Immunohistochemical mapping of amylin receptor components in the adult rat brain. C. BECSKEI[a], T. RIEDIGER[a], D. ZÜND[a], P. WOOKEY[b], T.A. LUTZ[a]. [a]*Institute of Veterinary Physiology, Vetsuisse Faculty of the University of Zurich, Switzerland;* [b]*Howard Florey Institute, University of Melbourne, Australia.*

Calcitonin receptors (CT-R) have previously been identified in specific regions of the rat CNS using in situ hybridization or autoradiography with iodinated ligands. The receptor activity modifying proteins (RAMP) alter the ligand specificity of the calcitonin receptors (CT-R) such that amylin, a member of the calcitonin (CT) family, is able to bind (CT-R + RAMP1 or CT-R + RAMP3). In the present study, the results of immunohistochemical mapping of CT-R is reported, using a potent and recently developed antibody that recognizes an intracellular epitope of the rat CT-R and high resolution immuno-fluorescence techniques. Abundant expression was found in the brain, with highest densities in the nucleus accumbens, lateral arcuate nucleus, lateral substantia nigra, bed nucleus of the stria terminalis, locus coeruleus, area postrema, nucleus of the solitary tract, and some of the nuclei of the reticular formations. These results are in close correspondence with previous mapping studies. However, we detected CT-R immunoreactivity in several additional brain areas, e.g. ventromedial, lateral and posterior hypothalamus, where CT binding has not yet been described. RAMPs were also localized in the area postrema by immunohistochemistry and in situ hybridization. Peripheral amylin is supposed to reduce feeding and gastric emptying via receptors on CT-R positive neurons of the area postrema. Our detailed mapping of the CT-R in the rat brain has identified CT-R positive cells that will be important for subsequent mapping of behavioral functions associated with the actions of CT-related peptides.

Exercise and energy balance: lessons from the CCK-A receptor deficient OLETF rat. S. BI, T.H. MORAN. *Department of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205, USA.*

Otsuka Long-Evans Tokushima Fatty (OLETF) rats lacking CCK-A receptors are hyperphagic and obese. Because exercise has been demonstrated to affect food intake and dorsomedial hypothalamus (DMH) NPY levels, we assessed the effects of running wheel access on patterns of food intake, body weight, daily activity and gene expression for hypothalamic peptides in OLETF and control LETO rats. We found that running wheel access normalized OLETF food intake and meal sizes, and prevented increases in body weight, plasma glucose and leptin levels. When the wheel was blocked, OLETF rats' food intake was immediately increased. Blocking running wheel also resulted in increased body weight in OLETF rats, but their weight did not reach those of unexercised OLETF rats. Compared to LETO rats, OLETF rats were more active in the running wheels. In LETO rats, NPY gene expression was increased in both arcuate and the DMH in response to running wheel access. In contrast, running wheel exercise increased arcuate but not DMH NPY expression in OLETF rats. Further, running wheel access reduced CRF expression in the paraventricular nucleus (PVN) in LETO rats. Relative to LETO rats, OLETF rats had decreased PVN CRF expression, which was prevented by running wheel access. Blocking the wheel resulted in lowered PVN CRF expression similar to that in control OLETF rats. Thus, voluntary exercise prevented the hyperphagia and obesity of OLETF rats, and had lasting effects on the eventual degree of OLETF obesity. How CCK signaling plays a role in exercise and energy balance remains to be determined. (Supported by DK57609. The OLETF and LETO rats were a generous gift of Otsuka Pharmaceutical, Tokushima, Japan.)

Amylin does not interact synergistically with cholecystokinin or insulin to inhibit gastric emptying in rats. M. BLECHA, R.D. REIDELBERGER. *VA Nebraska/Western Iowa Health Care System, Creighton University, and College of Saint Mary, Omaha, NE, 68105.*

The small intestinal peptide cholecystokinin (CCK) and the pancreatic hormones amylin and insulin have each been shown to decrease food intake. Recent work suggests that these peptides may interact synergistically to inhibit food intake. CCK and amylin also potently inhibit gastric emptying; thus, they may reduce food intake in part by interacting synergistically to decrease gastric emptying. The present study determined whether administration of amylin with either CCK or insulin reduces gastric emptying to a greater degree than the summation of their individual effects. Rats received a 20-min intravenous infusion of amylin (0, 0.2, 0.7, 2, 5 or 17 pmol/kg/min) with either CCK (0, 1.7, 5, or 17 pmol/kg/min) or insulin (0, 1, 3, 10, or 30 mU/h), and gastric emptying of saline was determined during the last 10 min of infusion. When administered alone, amylin and CCK each inhibited gastric emptying dose-dependently; minimal effective doses were 0.7 and 5 pmol/kg/min, respectively. Insulin did not reduce gastric emptying at any dose. Administration of amylin with either CCK or insulin reduced gastric emptying by an amount that was comparable to the summation of their individual effects. These data do not support the hypothesis that amylin interacts synergistically with CCK or insulin to inhibit gastric emptying. [Supported by the Department of Veterans Affairs.]

Amylin does not interact synergistically with cholecystokinin or insulin to inhibit food intake in rats. M. BLECHA, R.D. REIDELBERGER. *VA Nebraska/Western Iowa Health Care System, Creighton University, and College of Saint Mary, Omaha, NE 68105.*

The small intestinal peptide cholecystokinin (CCK) and the pancreatic hormones amylin and insulin have each been shown to decrease food intake. Recent work suggests that these peptides may interact synergistically to inhibit food intake. The present study determined whether administration of amylin with either CCK or insulin reduces food intake to a greater degree than the summation of their individual effects. At dark onset, non-food deprived rats received a 3-h intravenous infusion of amylin (0, 0.2, 0.6, or 2 pmol/kg/min) with either CCK (0, 1.7, 5, or 17 pmol/kg/min) or insulin (0, 1, 3, 10, or 30 mU/h). Food intake was determined from continuous computer recordings of changes in food bowl weight. When administered alone, amylin and CCK each inhibited food intake dose-dependently; minimal effective doses were 0.6 and 5 pmol/kg/min, respectively. Insulin did not suppress feeding at any dose. Administration of amylin with either CCK or insulin reduced food intake by an amount that was comparable to the summation of their individual effects. These data do not support the hypothesis that amylin interacts synergistically with CCK or insulin to reduce food intake. [Supported by NIH grant DK55830.]

Transient improvement of insulin sensitivity by hydroxycitrate (HCA) in fructose-induced insulin resistant rats. K. BRANDT, W. LANGHANS, M. LEONHARDT. *Institute of Animal Sciences, Swiss Federal Institute of Technology, 8603 Schwerzenbach, Switzerland.*

We examined long term effects of HCA on insulin sensitivity in rats fed a high fructose diet. After a period of restrictive feeding and 20% body weight loss, rats were given ad lib access to a 50% fructose diet supplemented with 3% HCA (CON = no supplements). We performed intravenous glucose tolerance tests (GTT) on ad lib days 0, 11 and 21, and an oral glucose tolerance test on ad lib day 27. On ad lib day 11, basal insulin was slightly decreased ($P = 0.074$), and the incremental area under the curve (iAUC) for insulin was markedly reduced ($P < 0.01$) in HCA rats. This diminished insulin response seemed to be related to a reduction in insulin secretion, as reflected by decreased C-peptide values. On ad lib day 21, basal insulin was reduced ($P < 0.05$) but the iAUC for insulin was unchanged in HCA rats. On ad lib day 27, neither basal insulin nor iAUC for insulin differed between HCA and CON rats. There were no treatment differences in basal glucose or iAUC for glucose in any of the GTTs. Interestingly, after 27 ad lib days rats pair-fed to HCA rats had the same amount of intra-abdominal fat, but basal insulin tended to be reduced compared to HCA rats ($P = 0.058$). Furthermore, liver fat was increased ($P < 0.0001$), whereas liver glycogen was decreased ($P < 0.05$) in HCA rats. These results suggest that the positive effect of HCA on insulin sensitivity, which may be mediated by a decrease in visceral adiposity, is diminished by adverse effects of HCA on liver metabolism.

Food intake and plasma ghrelin levels following central ghrelin administration in fatty Zucker rats. L.M. BROWN, D.J. CLEGG, S.C. WOODS. *Department of Psychiatry, Obesity Research Center, University of Cincinnati, Cincinnati, OH.*

Ghrelin is an orexigenic hormone secreted from the stomach and intestines. Ghrelin receptors are expressed on hypothalamic cells important in appetite and energy balance. We first determined that following a 48-h fast, plasma ghrelin increases (fed = 4063 ± 165.9 ng/ml; fasted = 5361.3 ± 519.2 ng/ml, $P < 0.05$), and 3rd-ventricular (i3vt) administration of ghrelin dose-dependently increases 1 h food intake (saline = 0.5 ± 0.05 g; 0.01 nm ghrelin = 1.92 ± 0.17 g; 0.1 nm ghrelin = 2.8 ± 0.13 g; 1.0 nm ghrelin = 4.5 ± 0.67 g) in Long-Evans rats. I3vt ghrelin also increased hypothalamic expression of AgRP and NPY mRNA (120% and 75%, respectively) as well as plasma ghrelin (40%). Although fatty Zucker rats had lower basal plasma ghrelin than Long-Evans rats (Zuckers 3481.8 ± 100.9 pg/ml, Long-Evans 4063 ± 165.9 pg/ml), i3vt ghrelin increased short-term food intake similarly in the two strains (Zuckers 4.45 ± 0.57, Long-Evans 4.55 ± 0.51), and plasma ghrelin did not change in the fatties. These data imply that whereas fatty Zucker rats eat more food following central ghrelin, the overall pattern of responding is deficient.

Resistin affects feeding behavior in rats. F. BRUGNOLI[a], C. POLIDORI[a], A. PATHAK[b], Y. DUROCHER[c], P. ROUET[b]. [a]*Department of Pharmacological Sciences and Experimental Medicine, University of Camerino, 62032 Camerino, Italy;* [b]*INSERM U586, Faculté de Médecine, 31073 Toulouse, France;* [c]*Animal Cell Technology Group, Biotechnology Research Institute, National Research Council Canada, Montreal, Canada.*

Resistin, a recently identified peptide, is secreted by adipocytes and is found in high levels in the serum of diet-induced obese mice. This peptide has been suggested to be the link between obesity and type II diabetes. The present study evaluated the effect of lateral ventricle recombinant resistin injection on feeding behavior of Wistar rats under different conditions: (1) when the animals were sated, (2) when their food intake was induced by either SHU9119 (0.1 nmol/rat) or NPY (3 nmol/rat) and (3) when the rats had been food deprived for 24 h. Single injection of resistin 0.1–0.2 nmol/rat did not reduce 24 h food intake of sated rats or that induced by SHU9119. On the other hand, resistin, at the dose of 0.2 nmol/rat, significantly reduced 2 h NPY-induced food intake ($6.6 + 0.3$ g vs $4.1 + 0.2$ g) as well as the 30 min feeding behavior following a 24 h food-deprivation ($5.88 + 0.6$ g vs $4.57 + 0.6$ g). Our data demonstrate that, in normal rats, resistin can affect NPY-related feeding behavior.

Dietary experience in childhood predicts overeating and dietary restraint in adulthood. J.M. BRUNSTROM, G.L. WITCOMB, T. BAGULEY. *Department of Human Sciences, Loughborough University, Loughborough, LE11 3TU, UK.*

Given the deleterious consequences of dietary restraint and overeating in adulthood, it is surprising that researchers have tended to focus on contemporaneous behavioural and physiological correlates of these activities rather than on their environmental aetiology. Our research addresses this problem. Specifically, we report results from four retrospective questionnaire studies. In each case, adult females were asked to recall their dietary experiences from between the ages of 5 and 10 years, together with information about current dietary behaviour. In Study 1 ($N = 242$), we found that measures of current (adult) dietary restraint and disinhibited eating (overeating) are related to memories of maternal dieting behaviour, control during mealtimes, and the use of food as a reward. In Study 2 ($N = 287$), we found that overeating (but not dietary restraint) is predicted by access to a high-energy diet during childhood. In Study 3 ($N = 175$), we explored the reliability of these findings and identify how maternal behaviour and childhood diet interact. In studies of this kind, it is important to consider the extent to which findings might be otherwise attributed to sources of systematic response bias. In Study 4 ($N = 261$), we introduced an alternative methodology that enables us to control statistically for potential sources of response bias. We also asked participants to identify the amount of lasagna, potatoes, cornflakes, and cheesecake, that they would normally select in an everyday meal. Consistent with our other results, we still find a reliable association between general meal-size selection in adulthood and access to high-energy foods in childhood. This association has not been identified previously and warrants further scrutiny.

The role of cognition in dietary learning. J.M. BRUNSTROM. *Department of Human Sciences, Loughborough University, Loughborough, LE11 3TU, England.*

Dietary learning is fundamental to normal dietary control because it facilitates both food selection and intake. Typically, learning is characterised as a form of classical conditioning. For example, 'flavour-nutrient learning' is regarded as a process whereby a novel tasting flavour (conditioned stimulus [CS]) becomes preferred or chosen after it has been paired with an energy-dense food (unconditioned stimulus [US]). Similarly, flavour-flavour learning occurs when a neutral flavour (CS) becomes liked (or disliked) after it is presented in close temporal proximity to an already liked (or disliked) flavour (US). Studies of dietary learning have tended to focus on animal behaviour. Indeed, there is a conspicuous paucity of data on learning in humans. To elucidate underlying processes it is important to observe clear and reliable instances of the phenomenon under scrutiny. Therefore, this bias towards animal research probably reflects the fact that human-based learning is regarded as a less robust phenomenon. However, one possibility is that human learning should not be regarded as a 'primitive' stimulus-driven process. Rather, failures to observe reliable instances of learning belie a more complex process that is sensitive to range of high-level cognitive processes. For example, evidence from our laboratory, and others, suggests that learning might be modulated by cognisance of CS-US relationships, attentional constraints, attitudes, and by dietary strategies such as dietary restraint. These possibilities are discussed, together with suggestions for future research.

Effects of basomedial hypothalamic injection of NPY-saporin on controls of food intake. K. BUGARITH, T.T. DINH, A.-J. LI, S. RITTER. *Programs in Neuroscience, Washington State University, Pullman, WA 99164-6520, USA.*

Neuropeptide Y-saporin (NPY-SAP) is a conjugate of NPY and the ribosomal toxin, saporin designed to lesion NPY receptor-expressing cells by selective NPY receptor-dependent internalization. We examined the effects of bilateral microinjection of NPY-SAP or blank-SAP control into the basomedial hypothalamus (BMH) on several specific controls of food intake. Feeding responses were tested to lateral ventricular administration of leptin (5 μg/5 μl/day for 3 days), ghrelin (2 μg/5 μl), glucagon-like peptide-1 (GLP-1, 5 μg/5 μl) and NPY (500 ng/100 nl) and to systemic administration of CCK (4 μg/kg), 2-deoxy-D-glucose (2DG, 200 mg/kg, sc) and 2-mercaptoacetate (MA, 68 mg/kg, ip). Effects of GLP-1 and CCK were assessed in 60- and 30-min tests, respectively, after an 18-h overnight fast. The lesioning effectiveness of the NPY-SAP was assessed by analysis of NPY, AGRP and CART mRNA and NPY and NPY-Y1 receptor immunohistochemistry. We found that NPY-SAP abolished leptin-induced reduction of feeding and body weight and ghrelin-induced stimulation of feeding, but did not impair the suppression of feeding induced by GLP-1 and CCK or the stimulation of feeding induced by NPY, 2DG and MA. Both AGRP/NPY and POMC/CART neurons, which are known to express NPY receptors, were destroyed by NPY-SAP. AGRP/NPY and POMC/CART neurons are considered to be primary mediators of ghrelin and leptin effects on food intake, while CCK, GLP-1, MA and 2DG have been shown to control feeding in part by mechanisms outside the BMH. Therefore, these findings show that BMH injections of NPY-SAP selectively impair controls mediated primarily by BMH neurons possessing NPY receptors, without causing widespread disruption of other ingestive behaviors. Results indicate the potential usefulness of NPY-SAP for chemical dissection of central neural circuits.

Interaction between β-3 adrenoreceptor and PPAR? variants in modulating energy compensation. J.E. CECIL[a], M.M. HETHERINGTON[f], W. WRIEDEN[c], P. WATT[d], C. BOLTON-SMITH[e], C. PALMER[b]. *[a]Departments of Psychology; [b]Biomedical Research; [c]Epidemiology and Public Health, University of Dundee; [d]Sport and Exercise Science, University of Brighton; [e]MRC Human Nutrition, University of Cambridge; [f]Psychology, University of Liverpool UK.*

The peroxisome proliferator-activated receptor γ (PPAR γ) is a crucial regulator of adiposity and energy balance. PPAR γ is important in differentiation of fat cells from fibroblasts and muscle, and polymorphisms located within this gene have been linked to obesity. Other candidate obesity genes include β-adrenoreceptor (BADR) subtypes (β-3), UCP2 and UCP3. This study investigated whether common variants in these genes were associated with eating behaviour. Subjects included a *PPARG* variant enriched sub-cohort of children ($n = 80$) aged 4–9 years. Ad libitum food intake from a test-meal was measured, 90 min following ingestion of either a no energy (NE: 250 ml water), low energy (LE: 187 kcal) or high energy (HE: 389 kcal) preload. LE and HE preloads consisted of 56 g muffin + 250 ml orange-juice. Satiety was assessed by a model of energy compensation, using a compensation index (COMP-X) to determine the precision of caloric compensation. Analysis of COMP-X revealed no main effects of preload condition, sex or weight category (lean, overweight, obese) on ability to compensate at the test-meal. However, COMP-X was associated with gene model, with a significant interaction of Trp64Arg and C1431T in modulating COMP-X ($P = 0.001$). Poor COMP-X (<50%) was associated with the presence of a T1431 allele (of C1431T polymorphism), whereas good COMP-X (>50%) was associated with the presence of an Arg allele. Previous studies have shown an interaction between BADR3 and PPARG variants in modulating adult body weight, however this is the first study to suggest such a genetic interaction in modulating eating behaviour.

Intracellular signaling by phosphodiesterase 3B is involved in the food intake and body weight reducing effects of centrally administered insulin. J.B. CHAMBERS, D.J. CLEGG, L.M. BROWN, R.J. SEELEY, A.Z. ZHAO. *Department of Psychiatry, Genome Research Institute, University of Cincinnati, Cincinnati, OH, 45237-0506.*

We tested the hypothesis that the ability of centrally administered insulin to reduce food intake and body weight is regulated by the intracellular actions of phosphodiesterase 3B (PDE3B). Insulin functions within the hypothalamus as a signal of adipose stores, and when exogenous insulin is infused into the third cerebroventricle (i3vt), food intake and body weight are reduced. PDE3B has been shown to be a downstream mediator of insulin action peripherally and we hypothesized that it may be an important mediator of insulin action in the CNS as well. Therefore, we tested whether centrally administered insulin would reduce food intake in the presence of a PDE3 inhibitor, cilostamide. Male Long-Evans rats implanted with an indwelling cannula were used. Food was removed 5 h before lights off, rats were first injected i3vt with dimethyl sulfoxide (DMSO) or a subthreshold dose of cilostamide (10 μg), and then were injected 30 min later with saline or 8 mU of insulin, resulting in four groups: DMSO-SAL, DMSO-INS, CILOST-SAL, CILOST-INS. Food was returned at the onset of the dark, and intake was measured subsequently. Food intake at 4 h was reduced 34.9% in the DMSO-INS group compared to the DMSO-SAL group (3.98 ± 0.86 g vs. 6.11 ± 0.56 g). The CILOST-INS group showed an attenuated reduction in food intake compared to the DMSO-INS group (5.36 ± 0.83 g vs. 3.98 ± 0.86 g). Our results indicate that the PDE3 inhibitor cilostamide reverses the body weight and food intake reducing effects of insulin, providing evidence of a role for the PDE3B pathway in the CNS actions of insulin.

Stress-induced bingeing after a history of restriction involves opioidergic sensitization. P.C. CHANDLER, P.K. WAUFORD, J.B. VIANA, C.R. MALDONADO, K.D. OSWALD, M.M. BOGGIANO. *Department of Psychology, University of Alabama at Birmingham.*

We found that footshock stress causes SIBAR (stress-induced bingeing after a history of restriction). To explore the possibility of opioid-receptor dysfunction in these SIBAR rats, we tested their response to 1.0 mg/kg ip naloxone HCl and to 8.0 mg/kg butorphanol tartrate, an opioid-receptor antagonist and agonist, respectively. All rats were injected 2 h after exposure to the shock alley, while sated but prior to bingeing. In both tests, SIBAR rats ate more PF than control groups (No-Stress/No-Restriction, Stress-only, and Restriction-only groups) after saline ($P < 0.001$ at 2 and 4 h; $P < 0.05$ at 24 h). However, their PF intake was most profoundly suppressed by naloxone, reducing it by 64%, 59%, and 40% vs. by 25%, 29%, and 8% in the controls at 2, 4, and 24 h post injection, respectively. Essentially, opioid-receptor blockade 'normalized' PF intake of SIBAR rats. Failure of these rats to compensate for typically short-lived naloxone-induced suppression by 24 h may indicate that opioidergic sensitization is necessary for bingeing. SIBAR rats were also the most sensitive to butorphanol-induced stimulation of food intake, increasing PF by 35%, 56%, and 35% vs. by 9%, 13%, and 17% in the controls at 2, 4, and 24 h post injection, respectively. Chow intake was unaffected by both drugs. This suggests a neuroadaptive process caused by caloric-restriction that involves super-sensitization of opioid-receptors to enhance reward-driven food intake. Opioid receptor sensitization may explain how stress and/or junk-food, both of which elevate endogenous opioids, trigger binge eating in humans. Supported by NEDA Laureate Young Investigator Award and NIH-R03-DK066007-01.

ICV infusion of MTII increases activity of neurons in the anterior PVN. P.C. CHANDLER, J. DEBERRY, J.E. COX, A. RANDICH. *Department of Psychology, University of Alabama at Birmingham.*

Infusions of MTII into the cerebral ventricles and the paraventricular nucleus of the hypothalamus (PVN) decrease food intake. We used adult male Sprague–Dawley rats to conduct single-cell recordings of PVN neurons prior to and following infusion of MTII (1 nmol/1 μl) into the lateral ventricle. Rats were paralyzed, artificially ventilated, and anesthetized during recording. A 5-min baseline recording period preceded the MTII infusion and the recordings continued for 60 min post-infusion. The data were grouped according to whether the site of recording was within or outside the PVN and its location relative to bregma (0.9 mm to approximately 2.1 mm posterior to bregma). The results showed that ICV infusion of MTII increased the activity of neurons located in the PVN 0.9 to 1.3 mm posterior to bregma. An ANOVA revealed a group (HIT vs. MISS) by time interaction for locations 0.9 and 1.3 mm posterior to bregma ($P < 0.05$). Post-hoc comparisons of means obtained at 60 min post-infusion revealed that neuronal activity was significantly greater in the HIT compared to the MISS groups at both 0.9 and 1.3 mm posterior to bregma ($P < 0.05$). The present results extend those of other studies by implicating the PVN in mediating the anorectic effects of melanocortins. More specifically, these results point to the involvement of the anterior parvocellular region of the PVN. Furthermore, these results parallel those of an earlier study (AJP, 286, R166-R173, 2004) in which we showed that intestinal infusions of lipids also increase neuronal activity specifically in this region of the PVN.

Effects of ghrelin on gastric emptying of peptone, Intralipid, and polycose in rats. P.K. CHELIKANI, R.D. REIDELBERGER. *VA Nebraska/Western Iowa Health Care System and Creighton University, Omaha, NE 68105.*

Ghrelin is an orexigenic gastric peptide that has been shown to accelerate gastric emptying. We determined the effects of ghrelin on gastric emptying of peptone, Intralipid, and polycose. Rats received a 20-min intravenous infusion of ghrelin (0, 15, 50 or 150 pmol/kg/min); 5 ml of saline, peptone (1.75 or 3.5 kcal), Intralipid (1.25 or 2.5 kcal), or polycose (2, 3 or 4 kcal) was rapidly instilled 10 min after infusion onset, and the volume emptied from the stomach was determined 10 min later. Nutrients induced a dose-dependent inhibition of gastric emptying. Volumes emptied were: saline (3.8 ml), peptone (1.9 and 0.8 ml for 1.75 and 3.5 kcal), Intralipid (2.9 and 2.1 ml for 1.25 and 2.5 kcal), and polycose (2.8, 2.6, and 1.9 ml for 2, 3, and 4 kcal). Ghrelin administration at 15, 50, and 150 pmol/kg/min accelerated emptying of saline by 6% at each dose. Ghrelin at 15, 50, and 150 pmol/kg/min increased emptying of peptone (3.5 kcal) by 97, 116, and 87%, respectively. Ghrelin at 15 and 150 pmol/kg/min also increased emptying of a lower dose of peptone (1.75 kcal) by 30 and 35%, respectively. Ghrelin at 150 pmol/kg/min had no effect on gastric emptying of Intralipid (1.25 and 2.5 kcal) or polycose (2, 3 and 4 kcal). These data suggest that ghrelin accelerates gastric emptying of protein, but has no effect on rate of gastric emptying of fat or carbohydrate. [Supported by the Department of Veterans Affairs].

Ghrelin attenuates amylin-induced inhibition of gastric emptying and food intake in rats. P.K. CHELIKANI, R.D. REIDELBERGER. *VA Nebraska/Western Iowa Health Care System and Creighton University, Omaha, NE 68105.*

Ghrelin is an orexigenic gastric peptide that has been shown to accelerate gastric emptying, whereas amylin is an anorexigenic pancreatic peptide that inhibits gastric emptying. We investigated the interaction of ghrelin and amylin on gastric emptying and food intake. Rats received a 20-min intravenous infusion of ghrelin (0, 15, 50 or 150 pmol/kg/min) with amylin (0 or 5 pmol/kg/min), and gastric emptying of saline was determined during the last 10 min of infusion. Amylin inhibited gastric emptying by 38%; ghrelin at 50 and 150 pmol/kg/min attenuated this response by 51 and 74%, respectively. Ghrelin at 15 pmol/kg/min had no effect on amylin-induced inhibition of gastric emptying. At dark-onset, non-food-deprived rats received a 3-h intravenous infusion of ghrelin (0, 15 or 50 pmol/kg/min) with amylin (0 or 2.5 pmol/kg/min), and food intake and meal patterns were determined from continuous computer recordings of changes in food bowl weight. Ghrelin infusion alone had no effect on food intake. Amylin decreased 3-h cumulative intake by 33%; ghrelin at 50 pmol/kg/min attenuated this response by 38%. In this experiment amylin decreased food intake by decreasing meal frequency and ghrelin attenuated this response by increasing meal frequency. Ghrelin at 15 pmol/kg/min had no effect on amylin-induced inhibition of food intake. These data demonstrate that ghrelin attenuates amylin-induced inhibition of food intake and gastric emptying with a similar potency. [Supported by: Department of Veterans Affairs and NIH grant DK55830].

Ghrelin attenuates the inhibitory effects of cholecystokinin and peptide YY (3–36) on gastric emptying in rats. P.K. CHELIKANI, A.C. HAVER, R.D. REIDELBERGER. *VA Nebraska/Western Iowa Health Care System and Creighton University, Omaha, NE 68105.*

Ghrelin is an orexigenic gastric peptide that has been shown to accelerate gastric emptying, whereas cholecystokinin (CCK) and PYY (3–36) are anorexigenic small intestinal peptides that inhibit gastric emptying. We investigated the interactions of ghrelin with CCK and PYY (3–36) on gastric emptying. Rats received a 20-min intravenous infusion of ghrelin (0, 15, 50 or 150 pmol/kg/min) with CCK (0, 17 or 50 pmol/kg/min) or PYY (3–36) (0, 17 or 50 pmol/kg/min), and gastric emptying of saline was measured during the last 10 min of infusion. Ghrelin at 15, 50 and 150 pmol/kg/min attenuated CCK (17 pmol/kg/min)-induced inhibition of gastric emptying by 14%, 39%, and 44%, respectively. Ghrelin at 50 pmol/kg/min also attenuated by 12% the inhibition of gastric emptying caused by a higher dose of CCK (50 pmol/kg/min). Ghrelin at 50 and 150 pmol/kg/min attenuated PYY (3–36) (50 pmol/kg/min)-induced inhibition of gastric emptying by 21% and 24%, respectively; ghrelin at 15 pmol/kg/min had no effect. Ghrelin at 50 pmol/kg/min also attenuated by 14% the inhibition of gastric emptying caused by a lower dose of PYY (3–36) (17 pmol/kg/min). These data demonstrate that ghrelin attenuates the inhibitory effects of CCK and PYY (3–36) on gastric emptying. [Supported by the Department of Veterans Affairs].

Comparison of the effects PYY (1–36) and PYY (3–36) on gastric emptying and food intake in rats. P.K. CHELIKANI, A.C. HAVER, R.D. REIDELBERGER. *VA Nebraska/Western Iowa Health Care System and Creighton University, Omaha, NE 68105.*

We compared the effects of the two molecular forms of the small intestinal peptide PYY, PYY (1–36) and PYY (3–36), on gastric emptying and food intake. Rats received a 20-min intravenous infusion of PYY (1–36) (0, 1.7, 5, 17, 50, 100, or 170 pmol/kg/min) or PYY (3–36) (0, 0.5, 1.7, 5, 17, 50, 100, or 170 pmol/kg/min), and gastric emptying of saline was measured during the last 10 min of infusion. The minimal and maximal effective doses (pmol/kg/min), and their inhibition (%) of gastric emptying, were 17 (11%) and 170 (38%) for PYY (1–36), and 5 (10%) and 170 (57%) for PYY (3–36), respectively. In feeding experiments, non-food-deprived rats received at dark onset a 3-h intravenous infusion of PYY (1–36) (0, 1.7, 5, 17, or 50 pmol/kg/min) or PYY (3–36) (0, 0.5, 1.7, 5, 17, or 50 pmol/kg/min). Food intake was determined from continuous computer recordings of changes in food bowl weight. The minimal and maximal effective doses (pmol/kg/min), and their inhibition (%) of 3-h cumulative food intake, were 17 (13%) and 50 (27%) for PYY (1–36), and 5 (19%) and 50 (43%) for PYY (3–36), respectively. These data indicate that: (1) PYY (3–36) is more effective and potent than PYY (1–36) in inhibiting gastric emptying and food intake, (2) for each peptide the potency and efficacy for inhibiting gastric emptying and food intake are similar, and (3) the anorexic effects of both peptides may be mediated in part through inhibition of gastric emptying. [Support by: Department of Veterans Affairs and NIH grant DK55830].

One month cigarette smoke exposure reduces body weight, appetite and hypothalamic neuropeptide Y in mice. H. CHEN#, R. VLAHOS, M. HANSEN, J. JONES, S. BOZINOVSKI, G. ANDERSON, M. J. MORRIS. *Departments of Pharmacology and Medicine, and CRC for Chronic Inflammatory Diseases, The University of Melbourne, 3010 Australia.*

Although nicotinic receptors have been demonstrated in hypothalamic appetite regulating areas, and nicotine inhibits food intake in animals, the mechanisms underlying the effects of smoking on appetite circuits remain unclear. Neuropeptide Y (NPY) is produced in the arcuate nucleus and exerts orexigenic actions in the paraventricular nucleus (PVN). Conflicting effects of nicotine on brain NPY content were previously reported, while few studies have examined the effects of cigarette smoking. *Purpose:* We observed no significant effect of acute smoke exposure on NPY content in hypothalamic regions. Here we evaluated how more chronic cigarette smoking affects body weight, food intake and hypothalamic NPY peptide. *Methods:* Balb/c mice (6 weeks) were exposed to smoke generated from 1 cigarette, 3 times a day for 4 weeks. Control mice were handled similarly without smoke exposure, and pair-fed mice were matched to the intake of the smoking group. *Results:* Food intake was decreased soon after smoke exposure began. After 4 weeks, smoking and pair-fed mice were significantly lighter than controls (22.0 ± 0.2, 23.2 ± 0.5, 24.9 ± 0.4 g, respectively, $P < 0.05$). Brown and white fat masses were reduced in the smoking group, but not in the pair-fed group, relative to control mice ($P < 0.05$). PVN NPY concentration was significantly reduced by smoke exposure, despite lower plasma leptin concentrations. Conclusion: 4 weeks exposure to cigarette smoke led to reduced body weight, food intake and adiposity. The selective reduction in PVN NPY concentration may contribute to the decreased appetite and reduced in body weight observed under these conditions.

Ketanserin blocked hypophagia, but not the PVN-pERK, induced by systemic 5-HTP in rats. S.H. CHOI, J.G. KIM, D.G. KIM, J.W. JAHNG. *Department of Pharmacology, BK21 Project for Medical Science, Yonsei University College of Medicine, Seoul, Korea.*

We previously reported that systemic 5-hydroxy-L-tryptophan (5-HTP) increases brain 5-HT level, decreases food intake and body weight gain in rats. Also, 5-HTP increased NPY expression in the arcuate nucleus and phosphorylated extracellular signal-related kinase (pERK) level in the hypothalamic paraventricular. The brain 5-HT level negatively correlates with the hyperphagic function of NPY. We examined if ketanserin, 5-HT 2A/2C receptor antagonist, inhibits both the 5-HTP induced hypophagia and ERK phosphorylation in the PVN. Male Sprague–Dawley rats (300–350 g) received an intraperitoneal 5-HTP (100 mg/kg) or saline 1 h before the onset of dark period. Ketanserin (1 mg/kg) given 30 min prior to 5-HTP blocked the hypophagic effect of 5-HTP either in 2 or 8 h intake. However, pERK induction by 5-HTP, which was determined by immunohistochemistry, was not changed by ketanserin pretreatment. These results indicate that 5-HTP induced hypophagia is mediated by 5-HT 2A/2C receptors, and suggest that ERK phosphorylation in the PVN may not be an anorexic signal, rather be an orexic, perhaps, induced by increased NPY expression in the arcuate, and that the brain 5-HT increased by 5-HTP administration may inhibit the transmission of this orexic signal at the PVN level, consequently induces hypophagia. Supported by KISTEP (JWJ).

Metabolic and behavioral responses to two caloric restriction paradigms in mice. A.L. CHRISTMAN, A.D. PARSONS, A.A. FOX, J.M. OVERTON. *Department of Nutrition, Food and Exercise Science, Florida State University, Tallahassee, FL 32306-4340.*

C57 mice were housed in room calorimeters for measurement of oxygen consumption (VO2) and assessment of locomotor activity and ingestive behavior. Mice were acclimated to thermoneutral temperature (30 °C) before undergoing caloric restriction (CR; 60% of ad lib consumption) for 2 weeks. CR was imposed by: (1) providing one feeding/d at the onset of the dark phase (Daily feeding; DF); or (2) providing the same number of calories in three feedings/week (Intermittent feeding; IF). After a few days, mice subjected to IF ate all calories provided in one day and were essentially fasted every other day. CR imposed by DF produced predictable and stable reductions in body weight and VO2, accompanied by a transient decrease in respiratory quotient (RQ; CO2/O2) reflecting fat mobilization that was most clearly evident in the light phase during the first week of CR. In contrast, CR imposed by IF produced marked oscillations in body weight, VO2 and RQ. On fasting days VO2 in the dark phase was much lower than for mice on DF; however, the very low VO2 reached during the light phase was similar for both groups of mice. On days when mice were fed during IF, subsequent light phase VO2 was similar to baseline levels while RQ was greater than 1.0 suggesting lipogenesis. Neither method of CR increased home cage locomotor activity. The results reveal markedly different metabolic and behavioral profiles in mice undergoing CR imposed by DF and IF. Supported by NIH HL56732.

Glycemia estimation as meal signal to order eating and spare insulin. M. CIAMPOLINI. *Firenze Università, Meyer Hospital, 50132 Firenze; Italy.*

89/120 healthy adults with dyspeptic, abdominal pain or diarrheic complaints trained estimation by at least 42 pairings of feeling hunger or discomfort during activity and measuring glycemia by glucometer They used this learned glycemia estimation by feelings to verify intake in the previous meal and prevent energy intake at high glycemia in the subsequent meal. 89 subjects and 31 controls reported 7-d-home diary at baseline in a 5 month prospective, randomized (3:1) investigation. The diary reported measurements before three mealtimes, which provided the 'glycemic average' (average preprandial glycemia in a week). The level of 4.55 mmol/l divided the subjects by 'glycemic average' in 46 low glycemia or LG group and 74 HG group. After training, only 3 of 34 trained LG subjects significantly decreased the 'glycemic average'; the entire group maintained the baseline means 'glycemic average', OGTT insulin area under curve (insulin AUC), HbA1c and body weight. The HG subjects had significantly higher 'glycemic average' (5.08 ± 0.43 vs. 4.26 ± 0.21 mmol/l), HbA1c (4.81 ± 0.44% vs. 4.50 ± 0.30%), insulin AUC (244 ± 138 vs. 180 ± 98 mU/l) though not body weight (66.8 ± 13.4 vs. 62.4 ± 11.1 kg, $P = 0.07$) than LG subjects at baseline. After training, 45/55 HG subjects reported significantly lower 'glycemic average' than baseline. All trained HG group decreased the mean 'glycemic average' (4.5 ± 0.43 mmol/l), diary SD, HbA1c (4.56 ± 0.47%) insulin AUC (164 ± 92 mU/l) and body weight (62.7 ± 12.1 kg) significantly more than the control group, reaching the levels in the LG group. At baseline and before any training, a consistent minority of the investigated population (LG group 38%) freely reported 'glycemic averages' within the range that was associated with the most accurate estimation and with insulin sparing. By 'glycemia estimation', the HG group (62%) was able to reach similar 'glycemic averages', insulin AUC and body weight.

Melanin-concentrating hormone (MCH)-induced water consumption is blocked by losartan, a specific angiotensin receptor antagonist. D.J., CLEGG, L.M., BROWN, S.C., BENOIT, K.L., TAMASHIRO, R., SAKAI, D., SALTER, A.G., WATTS, S.C., WOODS. *Department of Psychiatry, Obesity Research Center, University of Cincinnati, Cincinnati, OH.*

The lateral hypothalamus (LH) has a critical role in the control of feeding and drinking. Melanin-concentrating hormone (MCH) and orexin-A are expressed in separate neuronal populations in the LH, and each receives innervation from neuropeptide Y (NPY)-releasing axons. We assessed drinking and eating after the 3rd-ventricular (i3vt) administration of equally orexigenic doses of MCH (5 μg), NPY (7 μg) and orexin-A (3 μg). MCH stimulated proportionally more water than food intake, and when no food was available, MCH also had a significant dipsogenic effect (+2 ml). Orexin-A and NPY, in contrast, increased water intake only in proportion to food intake. Pre-treatment of rats with a low (subthreshold) dose of losartan, an angiotensin receptor antagonist, attenuated MCH-induced water consumption but had no effect on NPY or orexin-A-induced water consumption. Therefore, MCH-induced water consumption engages angiotensin receptors, but the water consumption associated with NPY and orexin-A does not. In 24-h water-deprived animals, NPY stimulated food intake in the absence of water (6.7 g in 1 h), whereas MCH and orexin-A did not (1.2 g in 1 h). In food-deprived but water-replete animals, MCH stimulated water consumption (11.5 ml in 30 min) whereas NPY and orexin-A did not (7.8 ml in 30 min). Hence, although both MCH and NPY stimulate food intake, NPY appears to be related more to food consumption per se and MCH more with water consumption. These results are also consistent with historical data linking activity of the LH with water intake the ARC to food intake.

Estrogen mediates hypothalamic sensitivity to adiposity signals and body fat distribution. D.J., CLEGG. *Obesity Research Center, Department of Psychiatry, University of Cincinnati, Cincinnati, OH.*

Body fat distribution differs between males and females and is associated with the levels of the 'adiposity' hormones, leptin and insulin. Females have more subcutaneous fat and higher plasma leptin whereas males have more visceral fat and higher plasma insulin. We previously reported that male and female rats are differentially sensitive to the anorexic actions of insulin and leptin in the brain, with males more sensitive to low doses of insulin and females more sensitive to low doses of leptin. To determine the role of gonadal steroids in central sensitivity to insulin and leptin, we gonadectomized male and female rats, implanted estradiol pellets subcutaneously and ventricularly, and assessed sensitivity to centrally administered leptin and insulin. Ovariectomy (ovx) decreased sensitivity to leptin administered into the 3rd ventricle (i3vt). Conversely, ovx changed sensitivity to i3vt insulin and increased visceral adiposity. Castrated males were less sensitive to i3vt insulin and more sensitive to i3vt leptin than intact males. Estradiol increased leptin sensitivity and decreased insulin sensitivity in both castrated and intact male rats. Following castration or estrogen administration, males had increased subcutaneous fat. These data suggest that gonadal steroids determine body fat distribution and sensitivity to centrally administered leptin and insulin.

Weight gain, hyperphagia and adiposity following Olanzapine treatment does not significantly influence circulating leptin in rats. G.D. COOPER[a], L.C. PICKAVANCE[b], A.J. GOUDIE[a], J.P.H. WILDING[c], J.C.G. HALFORD[a]. *[a]School of Psychology; [b]Department of Veterinary Preclinical Sciences; [c]Department of Diabetes and Endocrinology. University of Liverpool, UK.*

Weight gain and adiposity is a major undesirable side effect of some atypical antipsychotics. We have reported that olanzapine (OLAN)-induced weight gain can be modelled in rats (Goudie et al., J Psychopharmacol 16 (2002) 291–296). The present study explored further the relationship between weight gain, adiposity and endocrine factors such as endogenous leptin. 56 female Han Wistar rats, singly housed, were administered OLAN chronically b.i.d. (i.p), at doses of 0, 1, 2, and 4 mg/kg over 21 days. Total daily Food Intake (FI) was recorded. On day 21 animals were sacrificed. The perirenal fat pads were removed and trunk blood collected for assay. OLAN produced an inverted U-shaped dose-response curve for its effect on weight gain. The 1 and 2 mg/kg doses induced highly significant weight gain relative to vehicle. Total FI was significantly greater for the 1 and 4 mg/kg groups compared to vehicle. All OLAN treated groups displayed significantly larger perirenal fat pads, demonstrating increased adiposity. In contrast plasma leptin levels were only marginally elevated. This study extends our previous report of OLAN-induced weight gain in rats. Furthermore weight gain was associated with increased adiposity and hyperphagia. However leptin levels did not significantly increase despite a marked trend. Insignificant changes in endocrinological factors in the rodent model did mirror those significant changes previously reported in the clinical setting (Kraus et al., Am J Psychiatry 156 (1999) 312–314). Our results suggest that prolonged OLAN treatment may be required in rodent models in order to observe the 'hyperleptinaemia' associated with OLAN-induced weight gain previously reported in humans.

Energetic factors in animal models of antipsychotic induced weight gain. M.B. COPE. *Nutrition Sciences, University of Alabama at Birmingham.*

A major health concern for patients suffering from schizophrenia is antipsychotic induced weight gain (AIWG). There are relatively few rodent or other animal models that describe this phenomenon. Precise mechanisms causing this side effect are not presently known and without adequate models, the energetic factors influencing AIWG cannot be investigated properly. During this presentation, Dr Cope will introduce and describe AIWG models that are currently available, give details from a set of mouse studies recently completed in his lab, and discuss how these models can be used to investigate the energetic factors involved with AIWG. All antipsychotic drugs tested in our mouse model caused significant increases in weight gain; however, only olanzapine and quetiapine were associated with significantly increased food intake during these studies. Body composition data showed that the weight gained in the olanzapine treated mice was associated with fat gain, but this association was not found in the other drug treated mice. Our model of AIWG shows a pattern similar to that reported in humans; however, more detailed energetic evaluations (resting energy expenditure, activity levels, energy intake, etc.) of this model will be required to determine the underlying energetic factors involved with AIWG.

Baclofen reduces fat intake in 'bingeing' rats. R. CORWIN, F.H.E. WOJNICKI, A. BUDA-LEVIN. *Nutritional Sciences Department, Penn State University, University Park, PA 16802, USA.*

The GABA-B agonist baclofen reduces drug self-administration in rats. Given the co-morbidity between bingeing and substance abuse, we tested baclofen (0, 0.3, 0.6, 1.0, 1.8 mg/kg, i.p.) in a shortening binge protocol we developed. Twenty male Sprague–Dawley rats were used. Binge (B) rats ($n = 10$) had continuous access to chow (PMI 5001, LabDiet, Richmond, IN) 7 days a week and 2 h access to a bowl of shortening (Crisco, JM Smucker, Orrville, OH) every Monday, Wednesday, and Friday. Comparison (C) rats ($n = 10$) were maintained on a different protocol in each study. Study 1: C had continuous access to chow but no access to shortening. Study 2: C was maintained on the same diet protocol as B. Study 3: C had continuous access to chow and 2 h access to the shortening option seven days a week. Study 4: C had continuous access to chow and 2 h access to shortening on Mon, Wed, and Fri. However, on injection days, no chow was available to the C group during the 2 h shortening-access period. Baclofen reduced shortening intake in all studies ($P < 0.05$) at dosages that had no effect on or increased chow intake ($P < 0.05$). These results indicate that the baclofen-induced reductions in shortening intake were not due to non-specific behavioral disruption, and were not affected by the simultaneous availability of another food (chow). GABA-B receptors may be involved in the consumption of fatty foods during discrete periods of time, such as occurs during a binge. Partially funded by PSGC-WISER; Penn State College of Health and Human Development.

Operant responding for shortening in non-food-deprived rats. R. CORWIN[a], F.H.E. WOJNICKI[a], D.C.S. ROBERTS[b]. [a]*Nutritional Sciences Department, Penn State University, University Park, PA 16802, USA;* [b]*Department of Physiology and Pharmacology, Wake Forest University School of Medicine, Winston-Salem, NC 27157, USA.*

Progressive-ratio (PR) schedules of reinforcement have been used to assess the reinforcing effects of drugs and sweet foods. However, to our knowledge, PR schedules have never been used to assess the reinforcing effects of fat. Solid fat (shortening) is of particular interest because it is preferred over oil (1) and it promotes binge-type eating in rats (2). We have developed a procedure in which shortening is used to reinforce operant responding. Eighteen non-food-deprived male Sprague–Dawley rats were trained to press a lever during 1 h sessions for shortening (0.12 g/reinforcer; 1.10 kcal/reinforcer; Crisco, JM Smucker, Orrville, OH) or food pellets (45 mg A1 pellets; 0.14 kcal/reinforcer; Research Diets, Inc., New Brunswick, NJ), or both, under an exponential PR (3), fixed-ratio (FR), or concurrent PR/FR schedule. PR responding for shortening was reduced when pellets were concurrently available ($P < 0.05$), but FR responding for shortening was unaffected by concurrently available pellets. Conversely, PR responding for pellets was unaffected by concurrently available shortening, but FR responding for pellets was reduced when shortening was concurrently available ($P < 0.05$). These results demonstrate that shortening can maintain operant responding, and that responding for shortening differs from responding for food pellets. In addition, both the reinforcement schedule and the availability of alternative reinforcers affect responding for shortening or food pellets. Partially funded by PSGC-WISER; HHD; REU.

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Comparison of feeding suppression by intragastric ethyl oleate and other macronutrients. J.E. COX, G.R. KELM, S.T. MELLER, A. RANDICH. *Department of Psychology, University of Alabama at Birmingham and Health Science Institute, The Procter and Gamble Company, Mason, OH.*

We previously reported that intragastric infusion of ethyl oleate (EO), the ethyl ester of oleic acid, reduced total caloric intake and body weight [Appetite 39 (2002) 71]. Here we report two experiments. Each compared suppression of food intake by EO with suppression by two other macronutrient formulations. In each experiment, male Sprague–Dawley rats ($N = 12$) underwent three four-day test blocks on consecutive weeks. Within each block, rats received bolus intragastric infusions (10 ml) of vehicle (1% Tween 80, 2% triglycerol monooleate) on the first two days and infusions of one of the macronutrients (10 ml, 15 kcal) on the next two days. Loads were administered 30 min prior to lights-out, at which time liquid diet (vanilla-flavored Boost, Mead-Johnson, 1 kcal/ml) was presented. Cumulative food intake was measured 23 h later. In the first experiment, 17% EO, 37.5% peptone (PEP, a protein digestate), and 37.5% maltodextrin (MD) were infused. In comparison with vehicle, both EO and PEP reduced total daily caloric intake (load plus food) by approximately 10 kcal ($P < 0.05$). MD was less effective ($P < 0.01$) and did not reduce caloric intake. The second experiment compared 17% EO, 17% oleic acid (OA), and 17% corn oil (CO). EO was the only lipid to reduce total caloric intake ($P < 0.05$) and was more effective than CO ($P < 0.05$). Results with OA were intermediate between the other two lipids and were not significantly different from either. These results showed that EO was more satiating than a model carbohydrate and triglyceride and was equivalent to a protein source, generally considered to have the greatest satiating potency of any of the macronutrients.

Inhibition of ANG II-induced behavior and Fos-ir by losartan. E.C. CREWS, N.E. ROWLAND, K.L. ROBERTSON. *Department of Psychology, University of Florida, Gainesville, FL 32611-2250, USA.*

Mice, unlike rats, do not drink water following administration of peripheral angiotensin (ANG) II. However, peripherally administered exogenous ANG II induces Fos-immunoreactivity (Fos-ir) in the subfornical organ (SFO) in mice. In this study, we first examined the inhibitory effect of peripheral administration of the AT-1 receptor antagonist, losartan, on ANG II-induced Fos-ir in the CD-1 mouse. Fos-ir induced by peripheral administration of ANG II was significantly inhibited by peripheral administration of losartan, showing that losartan does cross into the mouse SFO. In a second study, endogenous ANG II was genereated by treatment with furosemide (40 mg/kg). This induced substantial 0.15 M saline consumption (mean 2.3 ml/2 h) that was significantly inhibited by losartan administration (~0.3 ml/2 h). Fos-ir was induced in the SFO by furosemide treatment and this also was inhibited by peripheral administration of losartan. Endogenous peripheral ANG II appears to have an important role in salt appetite induced in mice by furosemide. Thus, as in rats, AT-1 receptors in the SFO do seem to be critically involved in some aspects of fluid intake in mice.

Ghrelin and neuropeptide Y: orexigenic and metabolic signaling molecules exhibit an interaction with urocortin in the paraventricular nucleus of the hypothalamus. P.J. CURRIE, A. MIRZA, A. MIHES, K. SRICHAROON, N. TAL, P. NIEDLE. *Department of Psychology, Barnard College, Columbia University, 3009 Broadway, New York, NY, 10025 USA.*

Ghrelin is proposed to play an important role in the regulation of energy homeostasis, one exerted at the level of the CNS. Central injections of ghrelin stimulate food intake, body weight gain and enhanced body fat mass deposition. It is further argued that the peptide interacts with other systems within the hypothalamus, including neuropeptide Y (NPY) neurons of the arcuate nucleus. In the present study we compared the feeding and metabolic effects of ghrelin and NPY when injected into the paraventricular nucleus (PVN). Doses of either peptide, as low as 10–20 pmol, stimulated eating and increased respiratory quotient (RQ) when injected at dark onset. While the orexigenic action of the two peptides appeared comparable, NPY evoked more sustained elevations in RQ (to values exceeding 1.0). At higher doses, the impact on RQ in terms of magnitude and duration of effect was comparable. The orexigenic action of either peptide appeared to be maximal at dark onset when compared to other points of the light-dark cycle and similar responses were observed in male and female rodents. PVN ghrelin injections also modestly reduced energy expenditure while neither peptide altered locomotor activity. Finally, pretreatment with urocortin (UCN) antagonized the feeding and metabolic effects of either peptide. In conclusion, PVN NPY and ghrelin stimulate eating and promote carbohydrate oxidation while inhibiting fat utilization. These effects are blocked by the CRH-related peptide UCN which alone suppresses appetite and promotes fat oxidation. Overall these findings are consistent with an interactive role of PVN NPY, ghrelin and UCN in the modulation of appetite and energy metabolism.

Sex differences in Furosemide-induced NaCl and water intake by rats: relation to plasma volume and Na^+ concentration. KATHLEEN, S., CURTIS, CAROLINA M. HERRERA, JENNIFER L. TANNER, JENNIFER M. STRATFORD, ERIC G. KRAUSE, ROBERT J. CONTRERAS. *Department of Psychology and Program in Neuroscience, Florida State University, Tallahassee, FL 32306, USA.*

Sex differences in NaCl intake by rats after treatment with the natriuretic/diuretic drug, Furosemide, become more pronounced after multiple Na^+ depletions and are not attributable to differences in circulating levels of renin or aldosterone. This study examined NaCl and water intake, plasma Na^+ concentration (pNa), and plasma volume (indicated by plasma protein concentration; pPro) after Furosemide treatment in male rats and in ovariectomized (OVX) rats with or without estrogen (EB) replacement. Although EB-treated OVX rats had greater pPro and reduced overnight water intake basally, there were no differences between EB- and vehicle-treated OVX rats in pPro, pNa, or overnight water intake after one Furosemide depletion. Compared to male rats, OVX rats consumed less water overnight, which may have contributed to a greater reduction in plasma volume and to higher pNa. OVX rats also drank substantially less water than did males during 2-bottle (NaCl and water) intake tests after multiple Furosemide depletions; however, OVX rats consumed more NaCl during these 2-bottle tests. Thus, Furosemide elicits greater NaCl intake and blunted water intake in OVX rats despite greater volume loss and attenuated hyponatremia. These results, together with previous reports that Furosemide stimulates comparable increases in plasma renin and aldosterone in males and females, suggest that estrogen-independent alterations in central activation may underlie sex differences in response to Furosemide-induced natriuresis/diuresis. Consistent with this idea, numbers of Fos immunolabeled cells in the subfornical organ after Furosemide were lower in both groups of OVX rats compared to those in male rats. Supported by NIH DC04785.

D-Cycloserine potentiates short-delay, but not long-delay, conditioned taste aversion. R.A. DAVENPORT, T.A. HOUPT. *Biological Sciences and Program in Neuroscience, Florida State University, Tallahassee, FL.*

D-Cycloserine (DCS) is a partial glycine agonist at the NMDA glutamate receptor site that facilitates both declarative and non-declarative memory tasks. In order to determine if DCS enhances conditioned taste aversion (CTA) learning, we administered DCS before the pairing of saccharin intake and LiCl injection and measured CTA expression with 2-bottle tests. Water-deprived rats were injected with DCS (15 mg/kg i.p.) 15 min prior to 10-min access to 0.125% saccharin. Rats were injected with LiCl (19 mg/kg i.p.) 25 or 60 min after DCS. Controls were injected with saline in place of DCS, or saline in place of LiCl. One day after conditioning, rats were given 24-h, 2-bottle preference tests for 14 days. Preference was calculated as saccharin intake over total intake. Controls showed no CTA when saccharin was paired with saline (pref: 0.9 ± 0.04), and only a moderate CTA after LiCl in the absence of DCS (pref: 0.4 ± 0.1, $P < 0.01$ vs. saline). In the presence of DCS, rats showed a stronger aversion after LiCl at 25 min (pref:0.06 ± 0.02, $P < 0.05$ vs. LiCl alone), but the same aversion after LiCl at 60 min (pref: 0.32 ± 0.1). These results were not due to the decay of DCS during the long-delay: when DCS was administered 60 min before a short-delay LiCl pairing, rats still acquired a potentiated CTA (pref: 0.2 ± 0.1) compared to a LiCl-pairing alone (pref: 0.5 ± 0.1, $P < 0.05$). We conclude that DCS enhances a CTA but is dependent on the timing of both the gustatory stimulus and the toxin, such that DCS potentiates short-delay but not long-delay pairing of saccharin and LiCl. We hypothesize that this is due to a priming effect of DCS on the NMDA receptor. Supported by a FSU Neuroscience Fellowship and NIDCD03198.

Concurrent measures of feeding and locomotion after psychostimulant drug treatments. K. DAVIS, P.J. WELLMAN, J.R. NATION, L. BELLINGER. *Psyc Dept, TAMU College Station, TX 77843-4235.*

Studies of drug actions on eating and locomotion are most commonly conducted in separate tests, thereby precluding the opportunity to compare the concurrent temporal profiles of drug action on eating and locomotion. Concurrent measures of eating and locomotion can be assessed using automated activity chambers (Accuscan Instruments) in which a food container is suspended via a leash from an overhead electronic balance (Ohaus Instruments: weigh-below option). Each container is packed with a palatable mash diet and positioned above the vertical activity beams at the left front of a cage. In the present work, we demonstrate the use of the concurrent procedure to assess the impact of the psychostimulant drugs cocaine or nicotine on eating and locomotion in rats. Activity measures and feeding (without food deprivation) were recorded every min during a 45 min test period (conducted during the 1st hour of the dark phase). Baseline mash intakes after saline injection ranged from 3–9 g/45 min. Injection of nicotine tartrate (0.8 mg/kg, salt) suppressed eating and forward locomotion for the first 10 min after injection. In the subsequent 35 min period, locomotion remained suppressed whereas feeding rebounded to near vehicle levels by the end of the 45 min session. In contrast, injection with 7.5 mg/kg cocaine produced a moderate suppression of eating during the 45 min test period, but induced hyperactivity throughout the test session. The concurrent measure procedure can dissociate the temporal profiles of drug action on eating and on locomotion.

The behavioral genetics of dietary density influences on eating. J.M. DE CASTRO. *Department of Psychology, University of Texas at El Paso, El Paso, TX, 79968.*

Dietary density affects short-term food intake in humans. High dietary density is associated with higher overall intakes and larger meal sizes. Little is known, however, heritable influences on preferences for diets varying in density and individual responsiveness to dietary density. The influence of heredity, familial environment, and individual environment on preferred levels of, and responsiveness to dietary density was investigated by obtaining 7-day diary reported nutrient intakes from 102 identical, 100 fraternal same sex, and 50 fraternal opposite-sex adult twin pairs who were living independently. Significant influences were found of the genes and individual environment, but not familial environment, on the mean dietary densities of the reported diets regardless of gender and whether drinks were included in the calculation of density. Responsiveness to dietary density was gauged by the correlations and slope of the regression between dietary density and meal size. There were no significant genetic or family environment contributions found for either of these responsiveness measures. Hence, one way that the genes appear to influence intake is by affecting the preferred levels of dietary density. Dietary density appears to influence intake as a result of its physical characteristics rather than to a genetically influenced responsiveness to density.

Altered sucrose preference in CCK-A receptor deficient rats. B.C. DE JONGHE[a], M. COVASA[a], A. HAJNAL[b]. [a]*Department of Nutritional Sciences, The Pennsylvania State University, University Park, PA 16802;* [b]*Department of Neural and Behavioral Sciences, The Pennsylvania State University, College of Medicine, Hershey, PA 17033.*

OLETF rats lack functional CCK-A receptors and readily develop hyperphagia and type-2 diabetes. Taste preference functions in OLETF rats have not been investigated despite a growing literature focusing on orosensory components that lead to increased meal size. This study addresses whether pre-diabetic OLETF rats exhibit an altered taste preference that may account for their higher intake compared to non-mutant LETO controls. To establish a sucrose preference profile, series of short access, two-bottle tests were performed in age matched OLETF and LETO rats. A range of sucrose concentrations (0.03, 0.1, 0.3, 1.0 M) were presented with a choice of water over eight consecutive days in two, one-hour sessions (1000 and 1500 h). Rat chow was available ad-libitum except during licking sessions. Pre-diabetic OLETF rats exhibited a greater preference for 0.3 and 1.0 M sucrose [$F(1,8) = 11.4$; $P < 0.01$, $F(1,8) = 6.66$; $P < 0.05$, respectively] than LETO controls. Preliminary tests with preferred sodium chloride solutions (0.03, 0.15 M) did not reveal differential preferences between strains. These results suggest that OLETF rats are markedly different in facilitating ingestion by sweet solutions compared to LETO controls. In addition to other abnormalities, an increased preference for palatable and high caloric meals may contribute to the development of hyperphagia and obesity in OLETF rats. Nevertheless, dissection of orosensory and postingestive components of sucrose's effects in the OLETF rats warrants further investigation. This study was supported by NIH grant DK065709.

Mineral intake by cell-dehydrated rats. L.A. DE LUCA, JR., D.T.B. PEREIRA, R.B. DAVID, R.C. VENDRAMINI, J.V. MENANI. *Departamento de Fisiologia e Patologia, Faculdade de Odontologia, UNESP, Araraquara, SP 14801-903, Brazil.*

Isotonic NaCl is ingested in addition to water by cell-dehydrated rats in two-bottle tests. The objective of the present work was to evaluate whether mineral intake in cell-dehydrated rat is specific for NaCl. Adult male Sprague Dawley–Holtzman rats had distilled water and four mineral solutions (0.01 M KCl, 0.05 mM CaCl, 0.15 M NaHCO3, 0.15 M NaCl) at palatable concentrations (Tordoff, Am. J. Physiol. 36 (1994) R470–R475) available for consumption (five-bottle test). Cell-dehydration was produced infusing 1.5 ml of NaCl solution (0.9-control, 1.5, 3.0, 6.0 and 12%) intravenously for 10 min and the intake was recorded for the next hour. NaCl concentration-dependent increase in 0.01 M KCl intake ($0.3 + 0.1$, $1.4 + 0.4$, $1.7 + 0.6$, $3.1 + 0.7$, $5.5 + 0.9$ ml/h, respectively, $n = 11$, $P < 0.05$) was observed. The ingestion of the other mineral solutions was not significantly altered compared to control. The ingestion of KCl was not related to serum potassium concentration. There was no mineral selection when solutions were offered simultaneously 1 h after subcutaneous injection of furosemide (early extracellular dehydration), in spite the increase in total volume intake. Therefore, (1) mineral intake induced by cell-dehydration is not specific for NaCl solution, (2) taste processing is different between cell- and early extracellular dehydration, and (3) the type of mineral solutions available influences the choice. Supported by: FAPESP, CNPQ, PRONEX

Implicit and explicit attitudes of cognitive restraint and body image on food intake. J. DEAL, S. PLUNKETT. *Department of Psychology, Southeastern Louisiana University, Hammond, LA.*

Recent exploration into the mechanisms of intake regulation has begun to focus on the influence of uncompensated factors in food intake regulation. Uncompensated factors are those that influence intake directly, however, are not reciprocally affected by the changes in intake. There are a host of uncompensated factors known to play roles in intake, among which are cognitive variables. This study investigates the influence of two important cognitive variables, body image and cognitive restraint on intake. The impacts of these variables on intake are addressed by evaluating individual's implicit and explicit attitudes on body image and cognitive restraint. Participants for this experiment were female students in psychology 101 at Southeastern Louisiana University, ranging in age from 18 to 55 years. Body dissatisfaction and dietary restraint were determined explicitly through the participant's performance on the Body Satisfaction Questionnaire and the Three-Factor Eating Questionnaire, respectively, and implicitly through their reaction times on a Stroop task. Individuals recorded intake for 7 days in diet diaries that have been used previously for the study of intake in the natural environment. Preliminary results indicate that: (1) There are independent influences of both explicit and implicit attitudes of cognitive restraint and body image on intake; (2) Individuals who are congruent in both implicit and explicit attitudes for body image consume less than individuals who are not congruent in these attitudes or are unrestrained eaters; (3) Individuals who only explicitly restrain food consume less than individuals who only implicitly restrain food or who are unrestrained; and (4) Cognitive restraint mediates the relation between body image and food intake.

Cognitive determinants of restraint and body image on food intake. J. DEAL, S. PLUNKETT, PHD. *Department of Psychology, Southeastern Louisiana University, Hammond, LA.*

Recent exploration into the mechanisms of intake regulation has begun to focus on the influence of uncompensated factors in food intake regulation. Uncompensated factors are those that influence intake directly, however, are not reciprocally affected by the changes in intake. There are a host of uncompensated factors known to play roles in intake, among which are cognitive variables. This study investigates the influence of two important cognitive variables, body image and cognitive restraint on intake. The impacts of these variables on intake are addressed by evaluating individual's implicit and explicit attitudes on body image and cognitive restraint. Participants for this experiment were female students in psychology 101 at Southeastern Louisiana University, ranging in age from 18 to 55 years. Body dissatisfaction and dietary restraint were determined explicitly through the participant's performance on the Body Satisfaction Questionnaire and the Three-Factor Eating Questionnaire, respectively, and implicitly through their reaction times on a Stroop task. Individuals recorded intake for 7 days in diet diaries that have been used previously for the study of intake in the natural environment. Preliminary results indicate that: (1) There are independent influences of both explicit and implicit attitudes of cognitive restraint and body image on intake; (2) Individuals who are congruent in both implicit and explicit attitudes for body image consume less than individuals who are not congruent in these attitudes or are unrestrained eaters; (3) Individuals who only explicitly restrain food consume less than individuals who only implicitly restrain food or who are unrestrained; and (4) Cognitive restraint mediates the relation between body image and food intake.

Patterns of food and water ingestion during periods of deprivation in rats. M.J. DENBLEYKER, C.J. RICCARDI, T.A. HOUPT, J.C SMITH. *Psychology, Florida State University.*

It is known that when a rat is placed on a water restriction schedule, it will decrease its food intake, and conversely, when placed on a food-restricted diet, water intake is decreased. In contrast, the pattern of eating and drinking during food or water deprivation is not known. The present experiment measured the body weight and the microstructure of the ingestive patterns of 16 rats during periods of water or food deprivation. During the baseline phase before food or water restriction, the averages of food ingestion were 31 g of intake, 13 feeding bouts, 11 min for bout duration and eating at a rate of 0.2 g/min. Similar data for water were intake of 49 g, 17 drinking bouts, 2 min in duration at a rate of 1.5 g/min. When the animals were switched to the water-restricted schedule (water available for 1 h a day), they consumed only 63% of their baseline food intake and 47% of their baseline water intake. During water deprivation the decrease in food intake was not due to a decrease in number nor size of bouts, but to a decrease in rate of eating within a bout The rats had fewer drinking bouts, but the drinking bouts were significantly longer and the rate of drinking increased. During the food restriction phase (food was available for 1 h a day), animals consumed 44% of their average baseline food intake and 67% of their average baseline water intake. The rats had fewer, but longer, food bouts and ate at a higher rate per bout. The decreased water intake was due to a decrease in drinking bout length.

Dopamine in disturbances of food and drug motivated behavior: a case of homology? GAETANO DI CHIARA. *Department of Toxicology and Center of Excellence for Studies on Dependence, University of Cagliari, V.Ospedale 74,09142, Cagliari, Italy.*

Unfamiliar, highly palatable food and addictive drugs share the ability of stimulating dopamine (DA) transmission, as estimated by microdialysis, in the n.accumbens (NAc) shell. This property, however, shows quite differerent adaptive modulation for each one of these rewards. Thus, while the shell DA response to food undergoes single-trial, motivational state dependent and slowly reversible habituation, that to drugs,even to those that more closely mimick the action of food on DA transmission, as morphine,alcohol and nicotine, is fully resistant to habituation. Moreover, while food-induced stimulation of shell DA is strongly inhibited by pre-exposure to food-conditioned visual-olfactory stimuli, that to drugs is strongly potentiated by exposure to the same stimuli conditioned to the drug itself. Further differences between food and drug reward involve the DA stimulant properties of their associated stimuli. Thus, incentive food-conditioned stimuli stimulate DA transmission in the medial prefrontal cortex (PFCX) but fail to do so in the NAc shell; quite in contrast, the same stimuli, if conditioned to morphine or to nicotine, robustly stimulate DA transmission not only in the PFCX but also in the NAc shell. It thus appears that while the responsiveness of NAc shell DA to food undergoes negative adaptation upon exposure to primary and conditioned stimuli, that to drugs is adaptively regulated in an opposite, positive manner. These striking differences in adaptive regulation are likely to result in major differences in the influences exerted by DA on its cellular targets in the NAc shell. Indeed, the adaptive properties of NAc shell DA responsiveness to food obey pavlovian rules. On this basis it has been speculated that DA in the NAc shell subserves a role in pavlovian incentive learning, an hypothesis also corroborated by recent experimental evidence. If this is the case, addictive drug rewards and their associated stimuli, by dysadaptively driving the responsivenes of DA transmission,would overun rules critical for normal learning, thus initiating the process of addiction. In the same vein, one might also speculate that in affected individuals, an impairement of the adaptive mechanisms controlling the responsiveness of DA transmission in the NAc shell might provide the basis for certain disturbances in eating behavior characterized, like drug addiction, by compulsive responsiveness to conditioned incentives.

Reversal of diet-induced metabolic improvement in relation to phases of body weight loss. K. DIEPVENS[a], E.M.R. KOVACS[b], M.S. WESTERTERP-PLANTENGA[a]. *[a]Department of Human Biology, Maastricht University, P.O. Box 616, 6200 MD Maastricht; [b]Unilever Health Institute, Unilever R&D, Vlaardingen. The Netherlands.*

In general, weight loss seems to improve the metabolic profile. We investigated the relation between changes of metabolic parameters and phases of weight loss. 23 women (age 41.6 ± 10.0 years, BMI 27.7 ± 1.8 kg/m^2) participated in a 12-weeks moderate weight loss study (energy intake 60% of predicted energy expenditure (EE)), consisting of a phase 1 of 4 weeks followed by a phase 2 of 8 weeks. Resting EE (REE) and body composition were measured with a ventilated hood system and deuterium dilution. During phase 1 and 2, subjects lost, respectively, 2.5 ± 1.4 kg (BMI 26.8 ± 1.9 kg/m^2) and 1.8 ± 1.2 kg (BMI 26.1 ± 1.8 kg/m^2), while rate of weight loss was 0.09 ± 0.05 vs. 0.03 ± 0.02 kg/day ($P < 0.001$). Composition of body weight lost was 2.1 kg and 1.9 kg fat mass and 0.6 kg and 0.2 kg fat free mass (FFM) during phase 1 and 2, respectively. Reduction in REE was a function of reduction in % body fat ($P < 0.05$) during phase 1. Surprisingly, favourable changes in free fatty acids, triacylglycerol, *b*-hydroxybutyrate, glucose and total cholesterol in phase 1 were reversed in phase 2 ($P < 0.02$). Total ($r^2 = 0.32$) and LDL cholesterol ($r^2 = 0.18$) changed according to body weight loss during phase 1 ($P < 0.05$). Taken together, a negative energy balance resulting in modest weight loss induces an initial improvement in metabolic parameters. However, marginal weight loss thereafter reverses this improvement showing homeostasis of the metabolic parameters. A progressive sparing effect in FFM occurred.

Destruction of NPY-receptor-expressing neurons in the basomedial hypothalamus does not impair glucoprivic feeding. T.T. DINH, S. ROLAND, S. RITTER. *Programs in Neuroscience, Washington State University, Pullman, WA 99164-6520, USA.*

Neuropeptide Y (NPY) has been implicated in the glucoprivic control of feeding. The site of greatest orexigenic potency of exogenous NPY is the medial hypothalamus, and injection of NPY antibodies into this site reduces glucoprivic feeding (He and Edwards, 1998). Furthermore, glucoprivation increases NPY and Agouti gene-related protein (AGRP) mRNAs in the arcuate nucleus (Sergeyev et al., 2000; Fraley and Ritter, 2003). Both this increased gene expression (Fraley and Ritter, 2003) and glucoprivic feeding are abolished by retrograde immunotoxic destruction of hindbrain catecholamine/NPY neurons that innervate this area. Therefore, medial hypothalamic NPY neurons may be critical downstream components of the pathway for stimulation of glucoprivic feeding activated by hindbrain afferents. Here we tested this hypothesis using NPY-saporin (NPY-SAP), a conjugate designed to lesion NPY receptor-expressing cells by selective NPY receptor-dependent internalization of the ribosomal toxin, saporin. NPY-SAP was microinjected bilaterally at two sites within the arcuate nucleus to destroy NPY neurons and neurons mediating postsynaptic effects of NPY throughout the basomedial hypothalamus (BMH). In a second group of rats, ibotenic acid was injected to produce a non-selective destruction of BMH cell bodies. Glucoprivic feeding was measured following 2-deoxy-D-glucose (2DG, 100, 200, 400 mg/kg, sc) injection. We found that glucoprivic feeding was not impaired in either lesion group. However, both lesions produced rapid-onset obesity and reduced NPY and AGRP mRNA expression in the BMH almost completely. Thus, BMH NPY-receptor expressing neurons, including arcuate NPY/AGRP neurons themselves, are not required for glucoprivic feeding. Since hindbrain catecholamine/NPY neurons are required for glucoprivic feeding, this response must be mediated by projections of these hindbrain neurons to sites outside the BMH.

Estrous-related changes in ingestive and locomotor activity in relation to changes in vaginal cytology across the rat's 4-day estrous cycle. D.P. DIXON, H.M. RIVERA, L.A. ECKEL. *Program in Neuroscience, Florida State University, Tallahassee, FL 32306.*

Food intake and activity level vary across the rat estrous cycle. Inconsistent or unspecified protocols for assessing estrous stage in relation to the lighting cycle has resulted in some ambiguity in literature regarding when such behavioral changes occur. To address this, we examined food intake, running wheel activity, water intake, sexual receptivity, and vaginal cytology at 3 h intervals across the estrous cycles of 7 sexually naïve, Long-Evans rats housed under a 12:12 h lighting cycle. Vaginal cornification, indicative of estrus, occurred for 24–27 h and was maximal 4 h before the end of the estrous stage. Increased activity and decreased food and water intake were associated with estrus compared to non-estrous stages. These behavioral changes were limited to the 12-h dark period of estrus. Vaginal metestrus occurred for 6–9 h during the dark phase following estrus. Vaginal diestrus occurred for 51–54 h and spanned 2 light and 2 dark phases. Vaginal proestrus occurred for 9–12 h during the light phase immediately preceding estrus. Food intake, water intake, and activity level were similar during these non-estrous stages. During these stages, feeding and locomotor activity occurred almost exclusively during the dark phase. These results suggest that the dark phase of the lighting cycle is the optimal time to conduct tests that examine estrous-related changes in behavior. These data also demonstrate the importance of specifying the time in which vaginal smears are obtained in relation to the lighting cycle and the time when behavioral tests are conducted. Supported by NIH Joint Neuroscience Predoctoral Training Grant (NIH, NIDCR, NIGMS, NIMH, NINDS, NINR) and MH 63787.

Inconsistent sweet-calorie pairings impair caloric compensation following sweet meals. A.M. DOERFLINGER, S.E. SWITHERS. *Department of Psychological Sciences, Purdue University, West Lafayette, IN 47907.*

The propensity for sensory attributes of a food to be dissociated from caloric consequences has risen in proportion to the increased use of artificial sweeteners and fat substitutes in the western diet (Polhamus, 2001). In the present study, experience with sweet taste stimuli and the caloric consequence was manipulated in peri-weanling rats, prior to the animal's establishing a long history of associations between food and its caloric consequences. Peri-weaning rats were randomly assigned to one of four groups. For two groups, sweet taste was always associated with calories, thus these groups were labeled the Consistent groups. In one of these groups, the sweet taste and calories were high (30% glucose and 30% sucrose). For the second group, the sweet taste and calories were low (10% glucose and 10% sucrose). For the remaining two groups, sweet taste was not always associated with calories, thus these groups were labeled the Inconsistent group. Animals in the High Inconsistent group received 30% glucose and 0.3% saccharin while animals in the Low Inconsistent group received 10% glucose and 0.3% saccharin. Our hypothesis was that exposure to inconsistent diet contingencies (i.e. sweet oral stimulus with no caloric value) would impair regulation of food intake following a sweet preload. The results demonstrated that intake following the sweet preload differed for animals that had previously received the Inconsistent experience compared to animals that had previously received the Consistent experience. Thus, learned relationships between pre-absorptive and post-absorptive expectations may be used to modulate intake, and interfering with such relationships may impair regulatory processes.

Bone and body composition of 40 inbred mouse strains. S.A. DOMAN, E.A. BYERLY, D.M. PILCHAK, A.A. BACHMANOV, D.R. REED, M.G. TORDOFF. *Monell Chemical Senses Center, Philadelphia, PA 19104, USA.*

The purpose of this study was to gain some basic information about the bone and carcass composition of mice. We used a Piximus II DEXA densitometer to measure bone mineral density, bone mineral content, the weight of carcass lean and fat tissue, and body weight of ~10 male and ~10 female mice of the 40 core mouse strains of the Mouse Phenome Project. The mice were ~16 week old and had been fed AIN-76A diet. There was a wide range of strain means for all measures collected. For example, the heaviest strains (KK/H1J and NON/LtJ) were ~3× heavier, had ~3× the carcass lean weight and ~7× the carcass fat than the lightest strain (MSM/Ms). In general, males were heavier and had more lean and fat mass than females but this was not always the case. There were few sex differences in bone mineral density and usually males had lower bone density than females (exception, PERA/EiJ). There were strong positive correlations among body weight, lean weight, and fat weight, and also between bone mineral density and content. Bone mineral density and content had stronger correlations with lean weight than fat weight. These data illustrate the broad diversity of bone and body composition found in mice. They will be useful for choosing progenitor strains for genetic mapping studies.

The effects of drinking spout orifice size on licking behavior in inbred mice. C.D. DOTSON[#], A.C. SPECTOR. *Department of Psychology and Center for Smell and Taste, University of Florida, Gainesville, Florida 32611-2250.*

The measurement of licking in rodents has proven its utility in the study of taste and ingestive behavior. Research has shown that licking can be influenced by a variety of variables. Using a lickometer (Davis Rig), we assessed the effect of drinking spout orifice size on the licking behavior of inbred mice [C57BL/6J, SWR/J, 129P3/J and DBA/2J; $n = 5$/strain] that were maintained on a water restriction schedule and tested in 30 min sessions. When licking from a single stationary tube with a small orifice (SO; 1.519 mm ± 1.61%), mice took roughly twice as many licks as that taken from a tube with a large orifice (LO; 2.699 mm ± 0.75%), but the total intake was approximately the same. SO-tube burst licks were ~2X > than LO-tube burst licks, but burst number did not significantly differ indicating that mice adjust their licking primarily within a burst to regulate their intake volume. Although there was a significant effect of orifice size on interlick interval, the magnitude of the difference was slight (1.99%). When licking was restricted to 5 s trials within a session in which orifice was not varied, mice took 60% more trials with the SO compared with the LO tubes, while increasing trial licks by 20%. Interestingly, when the orifice size was quasi-randomly varied within the session, LO-tube licking was > SO-tube licking, suggesting that water delivered from the two orifice sizes differs in its reinforcement efficacy. Caution should be used in selecting orifice diameters for measures of licking in rodents because variations in size can have striking effects on the behavior. Supported by NIDCD R01-DC04475.

Changes in food intake and microstructure of a meal in response to a physical stressor. T.M. DOVEY[a], M.F. BALL[a], K.G. CLARK[a], A. RODGERS[a], J. PINKNEY[b], J.C.G. HALFORD[a]. [a]*School of Psychology, University of Liverpool UK;* [b]*Diabetes and Endocrinology Research Group. University Hospital Aintree.*

A study was conducted to assess the effect of physical stress on food intake and feeding behaviour using a universal eating monitor (UEM). Participants ($n = 29$) were exposed to the cold pressor procedure and a non-stress inducing control in a repeated measures design. Biological measures, psychometric questionnaires and visual analogue scales were used to assess the stress response of the participants. The stressor (cold press technique) failed to induce any significant increase in blood pressure (systolic or diastolic); but increased heart rate in a subset of individuals. The psychometric tool (Spielburger State Anxiety Inventory) revealed that participants experienced a significant increase in perceived stress after the cold pressor. Exposure to this stressor did not significantly alter food intake in the participant group per se, however, it did significantly increase the intake of restrained eaters ($n = 13$) (restraint classified on both the Three Factor Eating Questionnaire and Dutch Eating Behaviour Questionnaire). Data from the UEM demonstrate that exposure to this stressor produced the classic sigmoidal curve on ratings of fullness (and other appetite ratings) during the meal. Kissileff and colleagues have previously reported this curve shape to be characteristic of bulimic women. This curve showed that, after the stressor participants experienced a rapid mid-meal shift in ratings of fullness compared to control. This study illustrates that the cold pressor is a reliable stress inducing technique, which in restrained eaters induces the previously reported phenomena of stress-induced over-consumption. However, the data from the UEM suggest that stress can alter the microstructure of feeding behaviour of both restrained and non-restrained eaters.

Meal-anticipatory hypothalamic neuropeptide Y. D.L. DRAZEN, A.D. STRADER, T.P. VAHL, R.J. SEELEY, S.C. WOODS. *University of Cincinnati College of Medicine, Cincinnati, OH 45237, USA.*

Because survival may depend on eating relatively large meals, an important adaptation is to minimize their impact by initiating anticipatory responses that lessen postprandial hyperglycemia. Examples of these anticipatory responses include pre-meal insulin secretion, reduction of metabolic rate, and elevation of body temperature. Neuropeptide Y (NPY) robustly increases food intake and body weight, and evidence suggests that NPY more accurately enables individuals to anticipate large meals and cope with their metabolic impact. Consistent with this, central administration of NPY elicits meal-anticipatory responses, and NPY $-/-$ mice have an increased latency to eat after fasting. We therefore hypothesized that hypothalamic NPY mRNA would increase prior to a scheduled large meal. Male rats were conditioned to consume all of their daily calories (as liquid Ensure) within the same 4-h period each day (meal-fed, at 1200 h) for 14 days. Control rats had continuous access to Ensure. Animals from each group were then sacrificed hourly starting at 0900 h. Meal-fed rats had significantly higher hypothalamic NPY mRNA prior to the scheduled meal than controls (represented as a % of 0900 values; 1000: 114 ± 10 and 86 ± 14; 1100: 140 ± 21 and 79 ± 11; 1200: 138 ± 21 and 92 ± 9; and 1300 h: 113 ± 6 and 71 ± 3, meal-fed and controls, respectively). There was a parallel increase in plasma ghrelin (1200 h: 2074 ± 92 and 951 ± 119 (ng/dL), meal-fed and controls, respectively), and plasma insulin rose in meal-fed rats at 1200 h. Collectively, these data suggest that hypothalamic NPY may function to mediate meal-anticipatory responses, rather than to simply increase food intake.

Melanin-concentrating hormone (MCH) stimulates intake of alcohol but not an isocaloric sucrose solution in rats. E.A. DUNCAN, S. C. WOODS. *Department of Psychiatry, University of Cincinnati, Cincinnati, OH, USA.*

MCH increases both food and water intake and has been implicated in the hedonic aspects of eating due to its connection with reward pathways. Moreover, there is evidence that MCH possesses anxiolytic properties. These characteristics made the peptide a likely candidate to modulate alcohol intake. We hypothesized that MCH would act as an anxiolytic and decrease the intake of alcohol, but stimulate the intake of an isocaloric sucrose solution through its orexigenic activity. Rats were trained to drink a 10% alcohol solution or an isocaloric sucrose solution using the sucrose fading technique. Following training, rats were anesthetized and surgically implanted with a ventricular (i3vt) cannula. After recovery, training continued to reinstate baseline consumption levels. MCH (1, 5, or 10 μg) or saline was injected into the third ventricle. Each rat received every treatment in counter-balanced order across days. Each injection day was separated by 3 non-treatment days to restore baseline drinking levels. Intakes of chow, caloric solution and fluid were assessed over 2 h. MCH significantly and dose-dependently increased alcohol intake as compared to baseline: 58.5 ± 10.9% (saline), 95.7 ± 15.2% (1 μg MCH), 115.3 ± 8.2% (5 μg MCH), 183.5 ± 37.7% (10 μg MCH) $P < 0.0016$, but had no reliable effect on sucrose intake: 99.9 ± 6.7% (saline), 89.3 ± 6.7% (1 μg MCH), 97.2 ± 7.4% (5 μg MCH), 112.0 ± 8.6% (10 μg MCH) $P < 0.0561$. Total caloric intake was significantly increased in the alcohol group: 92.3 ± 17.3% (saline), 250.3 ± 70.9% (10 μg MCH) $P < 0.0076$, and the sucrose group: 110.6 ± 10.1% (saline), 155.4 ± 15.4% (10 μg MCH) $P < 0.0024$, as compared to baseline intake levels. These results suggest that MCH enhances the self-administration of an addictive substance beyond its ability to increase the consumption of calories.

CCK-8 reduces ethanol self-administration in alcohol-preferring rats. D. ECONOMIDOU[a], R. CICCOCIOPPO[a], C. POLIDORI[a], N. GEARY[b], M. MASSI[a]. *[a]Department of Pharmacological Sciences and Experimental Medicine, University of Camerino, 62032 Camerino, Italy; [b]E.W. Bourne Behavioral Research Laboratory, White Plains, NY 10605, USA.*

Intraperitoneal (IP) injections of CCK-8 reduce voluntary 10% ethanol intake of Marchigian–Sardinian alcohol-preferring (msP) rats. The present study evaluated in msP rats the effect of IP injection of CCK-8 (0, 4, 8 and 12 μg/rat) on the self-administration of 10% ethanol or of the equicaloric solution of 14% sucrose. Animals were trained for 30 days in 30-min daily sessions to self-administer ethanol or sucrose in operant conditioning chambers, where 0.1 ml ethanol or sucrose was delivered following each bar pressing. Sucrose or ethanol were available only during the self-administration sessions. To train rats to self-administer ethanol a classic sucrose fading procedure was adopted. IP CCK-8 significantly reduced ethanol self-administration. The dose of 4 μg/rat significantly reduced ethanol self-administration from 41.3 + 3.3 to 30.0 + 5.7 lever pressing in 30 min ($P < 0.05$); control rats showed a higher lever pressing for sucrose (135.5 + 13.9 responses in 30 min) and IP CCK-8, 4 μg/rat, did not significantly modify the number of responses (107.5 + 13.7; $P > 0.05$). The dose of 8 μg/rat of CCK-8 significantly reduced both ethanol (57% reduction) and sucrose (41% reduction) self-administration; the dose of 12 μg/rat reduced ethanol self-administration by 72% and sucrose self-administration by 37%. These data suggest that CCK-8 reduces the reinforcing effects of ethanol and of sucrose that maintain self-administration; under these conditions this effect is relatively more pronounced for ethanol than for sucrose. Experiments are going on with lower concentrations of sucrose or saccharin to assess the selectivity of the effect on ethanol. This work was supported by NIH grant AA 12880.

Stepwise distension and cholecystokinin octapeptide (CCK-8) excited slowly adapting gastric mechanoreceptors in pigs. B.R. ELLISON#, W.W. BIGNELL, W.L. GROVUM. *Department of Biomedical Sciences, Ontario Veterinary College, University of Guelph, Ontario, Canada N1G 2W1.*

The aim was to evaluate the physiological significance of CCK as a satiety signal. CCK-8 injected intravenously has depressed food intakes in several species and has excited mechanoreceptors sensing gastric distension in rats. In our work, 17 Yorkshire pigs were fasted overnight and anesthetized with sodium pentobarbital. Activity from single vagal afferent fibers innervating slowly adapting gastric mechanoreceptors was isolated to examine the combined effects of gastric distension (0, 250, 500, 750 and 1000 ml air) and i.v. injections of CCK-8 (0, 0.06, 0.25, 1.0 and 4.0 μg/kg). The distensions were each imposed for 30 s in ascending order following each CCK-8 dose (also given in ascending order). Nine data sets were obtained from 8 receptors in 5 different pigs (43.2 ± 6.6 kg). The distensions alone (no CCK-8) produced 2.1^{a}, 4.2^{ab}, 6.3^{b}, 6.9^{bc} and 10.3^{c} impulses/sec ($P < 0.0001$) whereas the CCK-8 doses alone (no distension) produced 2.2^{a}, 3.7^{ab}, 4.3^{ab}, 6.2^{bc} and 8.7^{c} impulses/sec ($P < 0.0001$) respectively. In 5 receptors, the distension and CCK-8 effects were additive or synergistic whereas in the others, CCK-8 appeared to eliminate the effects of upper distension levels perhaps due to receptive relaxation. While the threshold effect of CCK-8 was 1.0 μg/kg statistically, a visual inspection of the data indicated the threshold may have been as low as 0.06 μg/kg in 6 pigs and 0.25 μg/kg in 2 others. These data support the recent findings of Kissileff et al. that subthreshold gastric distension and subthreshold intravenous CCK-8 infusions combined to reduce food intake in humans. Endogenous CCK may therefore contribute to satiety.

Habituation as a mechanism regulating food intake in humans. L.H. EPSTEIN. *Pediatrics, University of Buffalo, New York.*

Habituation is a basic property of the nervous system, and a substantial body of research has shown that animals and humans habituate to repeated presentations of food cues, and that habituation is related to ingestive behaviors. Subjects show decreases in both physiological and behavioral variables related to food intake, and presentation of novel food and non-food stimuli will recover initial responding. The rate of habituation is related to energy consumption in ad libitum eating conditions. Food variety reduces habituation, and also increases energy consumption. Non-food stimuli that alter allocation of attention act as dishabituators and stimulate food consumption, including stressors, and stimulus intensity relates to degree of dishabituation. Research suggests that reduction in motivation to eat may also be related to habituation, and dishabituators and variety alter both habituation and motivation to eat. Basic animal and human research provides brain mechanisms relevant to understanding how habituation may influence energy intake. The results provide a strong evidence base for the role of habituation in ingestive behavior. New directions in habituation research will be discussed. Research cited from our laboratory was funded by grants from NICHD, NIH.

Divergent response to caloric refeeding in Sprague–Dawley and Long Evans rats. S.A. EVANS, A.D. PARSONS, J.M. OVERTON. *Department of Nutrition, Food and Exercise Science, Florida State University, Tallahassee, FL 32306-4340.*

Male mature Sprague–Dawley (SD) and Long Evans (LE) rats were instrumented with telemetry transmitters for measurement of heart rate (HR) and housed in room calorimeters for assessment of food intake and oxygen consumption (VO2) at standard lab temperatures (23 °C). After baseline recording (body weight about 360 g), rats were assigned to either ad lib feeding or to caloric restriction (CR; 60% of baseline ad lib calories) for 2 weeks followed by a refeeding period. Ad lib rats had stable food intake (84–88 kcal/d) and gained weight at the rates of 3–4 g/d. Groups from both strains assigned to CR exhibited similar patterns of weight loss and reductions in VO2 and HR during CR. Upon refeeding, SD rats exhibited a transient hyperphagic response (one-day) accompanied by sustained suppression of VO2 and HR that remained evident 4 days after refeeding. In contrast, LE rats exhibited hyperphagia that was clearly still evident 4 days after refeeding accompanied by a complete normalization of HR and VO2 by the third day. Mean total intake during the 4 days of refeeding was greater in restricted LE rats (LE = 423 ± 14 kcal; SD = 372 ± 14 kcal; $P < 0.01$). The results reveal a divergent response to recovery from caloric restriction between these two strains. Therefore, we conclude that during recovery from CR, regulation of appetite and energy expenditure can occur independently. Supported by NIH HL56732.

Changes in body composition and metabolic adaptations during transition from a 14% to a 50% protein diet. P.C. EVEN, L. MAKHARIOS, J. MINET-RINGUET, S. DARE, J. FROMENTIN, D. TOME. *Unit INRA/INAPG 914 Nutr Physiol and Feeding Behavior, F75231 Paris cedex 05, France.*

Rats switched from a 14% (P14) to a 50% (P50) protein diet, adapt rapidly, are able to sustain growth and reduce body fatness. In this study we followed rats during the first 15 days of adaptation to a P50 diet and measured the changes induced on food intake, body composition, and glucose and insulin response to feeding. As previously observed, food intake was strongly reduced the first day of P50 feeding, but recovered as soon as the second day and stabilized at a 15% lower level (NS) than during P14 feeding. The follow up of the changes induced on body composition during P50 showed that the decrease in body fat occurred within four days. The weight of the adrenals and kidneys peaked after four days then decreased but was still higher than in P14 fed rats after 15 days. The changes induced on blood glucose and insulin after a calibrated test meal did not reveal any significant alteration of the glucose response, but showed that the insulin response was blunted after the ingestion of a P50 meal for the first time. Pre-meal insulin level was increased after 4 days of adaptation but normal again after 15 days (and reduced after 3 months). It is concluded that adaptation to a P50 diet induces a very rapid reduction in body composition (4 days). A critical period seems to occur between 1 and 4 days of adaptation as testified by a blunted insulin response to feeding the first days and an increase in blood insulin levels and a peak in adrenals weight after 4 days.

Adaptation in the components en energy expenditure during transition from a 14% to a 50% protein diet. P.C. EVEN, L. MAKARIOS, J. MINET-RINGUET, S. DARE, J. FROMENTIN, D. TOME. *Unit INRA/INAPG 914 Nutr Physiol and Feeding Behavior, F75231 Paris cedex 05, France.*

We have shown that rats switched from a 14% (P14) to a 50% (P50) protein diet exhibit a period of adaptation characterized by a very fast decrease in body fatness within four days and transient signs of metabolic stress as evidenced by an altered insulin secretion (first day) and increase in the adrenals weight (4 days and after). In this study, we investigated how the various components of energy expenditure (basal metabolism, thermic effect of food, protein glucose and lipid oxidation) evolves during this same period. We observed that the rate of protein oxidation was adjusted to the increased protein load within two days. This adaptation seemed to subsequently affect glucose metabolism as testified by an excessive dependency on carbohydrate oxidation in the post-absorptive state after 4 days. Surprisingly, adaptation to the high protein diet resulted in a decreased basal metabolism already visible after 4 days, and significant after 15 days. The thermogenic response to feeding was blunted in response to the first ingestion of the high protein diet, tended to be increased after one day of adaptation then returned to values equal or below those observed in rats fed the 14% protein diet. It is concluded that adaptation to a high protein diet occurs in two main steps: first by adjusting protein oxidation to protein intake (1–2 days), then by progressively adjusting carbohydrate metabolism (4–10 days). The decrease in basal metabolism and the absence of increase in the thermic effect of feeding under high protein feeding question the classical concept of dynamic specific activity of amino acids and requires that the cost of converting amino acids to glucose be reappraised.

Effect of high protein diet on central nervous system revealed by Fos protein activation. R. FAIPOUX, G. FROMENTIN, A. BENSAID, D. TOME. *Unit INRA/INAPG 914 Physiol Nutr and Feeding Behavior, F75231 Paris cedex 05, France.*

Transition from a normal (P/E 14%) to a high protein diet (P/E 55%) induces a depression in food intake the first day and a progressive return to the initial intake during the following days but the brains areas involved in these effects are still unknown. In the present study, C-fos activation was determined 90 min after a 2g-calibrated tested meal in different brain area in rats adapted to a P14 diet (control), or 24 h after transition from a P14 to a P55 diet. C-fos expression has been related with the activation of central areas supposed to be involved in regulation of food intake, i.e the nucleus of solitary tract, the hypothalamic area (dorso-median nucleus, ventro-median nucleus and arcuate nucleus), and the anterior pyriform cortex. Count of activated neurons showed that within the nucleus of the solitary tract, the P50 diet induced significantly higher activation than the P14 diet. In the hypothalamic area, the P50 diet also induced greater activation but only within the ventro and dorso-median nucleus. Finally, the P50 diet produced a higher activation in the anterior pyriform cortex than P14 diet. Moreover, each area has been divided into shorter segments, which allowed to precisely identify areas involved in high protein intake regulation.

Satiation of need-related sodium appetite in rats studied using progressive ratio schedules. L.J. FARNBAUCH, N.E. ROWLAND. *Department of Psychology, University of Florida, Gainesville, FL 32611-2250.*

Numerous studies have examined powerful mechanisms for induction of need-related sodium appetite in mammals. In contrast, the existence of mechanisms for satiation has been a matter of debate. This is in part because, following acute sodium depletion, rats often consume hypertonic NaCl solution in considerable fold excess of their physiological deficit. In the present study, we have examined the motivational characteristics of need-induced sodium appetite using operant schedules. Male Long-Evans rats (a strain that we have shown to consume 2–3 fold above their deficit when access to NaCl is cost-free) were given ad libitum access to distilled water and a natural ingredient low-sodium (~0.015%) diet, and received a daily injection of furosemide (5 mg/kg). These conditions induced a chronic sodium appetite that was stable from day-to-day. Depleted rats were first trained to lever press for access to NaCl solution (0.3 or 0.45 M) from a sipper spout that was retractable. They were then assigned to one of four groups, such that completion of a progressive ratio (PR) yielded either short or long (7.5 or 15 s) availability of the spout and the PR itself had either low or high steps (~1.25 vs 1.5-fold increments). The group given long salt access time (15 s) pressed significantly less (i.e. their breakpoint was lower) than the group given short salt access time (7.5 s). The total amount of NaCl consumed in each condition was close to the estimated physiological depletion. So, unlike free access conditions, the PR protocols reveal an accurate mechanism for satiation of sodium appetite.

Distinct forebrain and brainstem contributions to the NPY mediation of ghrelin hyperphagia in rats. L.F.H. FAULCONBRIDGE, H.J. GRILL, J.M. KAPLAN. *University of Pennsylvania, Department of Psychology, Philadelphia, Pennsylvania, USA.*

We had shown that a robust hyperphagic response is obtained with delivery of ghrelin to either brainstem (4th) or forebrain (3rd) ventricles. Here, we explore NPY mediation of ghrelin-hyperphagia elicited from either ventricle placement with and without an aqueduct grease plug that restricts CSF flow between the forebrain and brainstem ventricles. Without aqueduct occlusion, each icv-elicited response was reversed by prior administration of either a NPY Y1 receptor antagonist (1229U91; 5 nmol/1 μl) or a NPY Y5 receptor antagonist (D-Tyr^{27,36} D-Thr^{32} NPY$^{[27-36]}$; 10 μg/1 μl). Because of CSF flow, however, these observations do not address the anatomical sites of the ghrelin-NPY-R interactions. To determine whether the interactions are local (i.e. intrinsic to either the brainstem or hypothalamus) and/or involve long pathways, we provide all combinations (same and cross-ventricle) of ghrelin (150 pmol/1 μl) and NPY-R antagonist delivery where CSF flow is blocked by aqueduct occlusion. For brainstem ghrelin delivery, results were consistent with the brainstem-intrinsic model: 4th-icv pretreatment with either antagonist reversed the hyperphagic response, whereas 3rd-icv antagonist delivery was without effect. By contrast, NPY mediation of the 3rd-icv response to ghrelin entailed both long and short projections: the effect was reversed by 4th-icv Y1 antagonist delivery and by 3rd-icv Y5 antagonist treatment. The converse treatment conditions, 3rd-icv Y1-antagonist and 4th-icv Y5 antagonist treatment, were without effect. The contrasting patterns of ghrelin-NPY-R antagonist interaction demonstrate distinct mediating pathways (re, location and subtypes of relevant NPY receptors) for the hyperphagic responses triggered, respectively, by forebrain and CBS GHS-R stimulation. Supported by DK21397 and DK42284.

Social defeat increases food intake and body and fat masses in Syrian hamsters. M.T., FOSTER[a,*], M.B., SOLOMON[b,*], K.L. HUHMAN[b], T.J., BARTNESS[a,b]. [a]*Department of Biology, Georgia State University;* [b]*Department of Psychology, Center for Behavioral Neuroscience, Atlanta, GA 30303.*

Non-traumatic stress stimulates food intake and body/fat mass in many humans; however the opposite most often is true in non-human animals. In the social defeat paradigm, where a smaller animal is placed in the home cage of a larger resident aggressor, subordinate rats and mice show decreased food intake and body mass. This effect however has not been demonstrated in Syrian hamsters, which exhibit long lasting behavioral changes following social defeat. Therefore, we asked: Does repeated social defeat affect food intake and body/fat mass in male Syrian hamsters? Repeated social defeat significantly increased food intake and body/fat mass in subordinate (defeated) male hamsters compared with non-stressed controls, as well as significantly increasing white adipose tissue (WAT) pad masses (i.e., mesenteric, inguinal, epididymal and retroperitoneal WAT). In a second experiment we asked: What is the minimal amount of social stress necessary to produce significantly increased body mass and food intake? Although a single defeat did not significantly increase these measures, 4 or 8 defeats did. This is the first stress model in rodents using an ethologically relevant stressor to show increased food intake and body/fat mass and therefore may prove useful to gain insight into the mechanisms underlying stress-induced obesity in humans.

Supported by NIH R01 MH62044 to KLH, NIH R01 DK35254 to TJB and NSF IBN 9876495.

Effects of SFO disconnection on drinking and Fos expression in the rat brain following intragastric hypertonic saline. J.A. FREECE, J.E. VAN BEBBER, D.K. ZIERATH, D.A. FITTS. *Department of Psychology, University of Washington, Box 351525 Seattle, WA 98195-1525.*

Three circumventricular organs (CVOs) of the brain are suspected to contain osmoreceptors that drive hypothalamic and other nuclei to secrete vasopressin and to elicit drinking during hypernatremia: the subfornical organ (SFO), organum vasculosum laminae terminalis (OVLT) and area postrema (AP). We previously demonstrated that Fos-like immunoreactivity (Fos-ir) was nearly absent in the main body of SFO of rats with either sham cuts or knife cuts of the afferent and efferent connectivity of the SFO following a low dose of hypertonic saline (0.5% of body weight of 0.6 M NaCl by gavage). The present experiment repeated this method using a higher dose of saline (0.5% body weight of 1.5 M NaCl) so that Fos-ir would likely be expressed in CVOs of intact rats. If the Fos-ir was absent in SFO of knife-cut rats after osmotic loading, it would question the presence of independently functioning osmoreceptors in the SFO. In an initial test, knife-cut rats drank significantly less water than sham-cut rats after the osmotic load, thus confirming a role for the SFO in osmotic drinking. In a second test at least a week later the rats were not allowed to drink after the gavage and were perfused for analysis of Fos-ir at 90 min. Compared to sham-cut rats, the knife-cut rats displayed significantly elevated Fos-ir in the main body the SFO, dorsal cap of the OVLT, and ventral median preoptic nucleus after the hypertonic load. The knife cut significantly decreased Fos-ir in the supraoptic nucleus and in the medial and caudal parts of the AP of knife-cut rats. These findings strengthen the case for the presence of independently functioning osmoreceptors in the SFO. They also suggest that the Fos response in the AP after osmotic loading is dependent on the intact connectivity of the SFO.

The role of the gustatory cortex in drug- and sucrose-induced suppression of conditioned stimulus (CS) intake. R.I. GEDDES, L. HAN, P.S. GRIGSON. *PennState College of Medicine, Hershey, PA 17033.*

Rats suppress intake of a saccharin CS when paired with an aversive agent, a more rewarding sucrose solution, or a drug of abuse. The reward comparison hypothesis suggests that rats avoid intake of a CS cue following CS-drug pairings, because the value of the taste cue pales in anticipation of the rewarding properties of the drug (Grigson, 1997). Bilateral lesions of the gustatory thalamus selectively disrupt the reduction in CS intake following pairings with a rewarding sucrose solution (Reilly, 1996), a 10 mg/kg dose of cocaine (Baldwin, 2002), and a 15 mg/kg dose of morphine, but not with a matched dose of LiCl (Grigson, 2000). Similarly, Mackey (1986) showed that, bilateral lesions of the gustatory cortex block the reduction in CS intake following pairings with morphine, but not LiCl. Using similar bilateral lesions, the present study examined the role of the gustatory cortex in sucrose-, cocaine-, morphine-induced suppression and, LiCl-induced conditioned taste aversion. Lesions of the gustatory cortex fully prevented the suppressive effects of a rewarding sucrose solution and those induced by both a 15- and 30-mg/kg dose of morphine. The suppressive effects of cocaine were attenuated, but the lesion effect was overcome by using a higher dose of cocaine (20 mg/kg). While this lesion disrupts the suppressive effects of sucrose, morphine, and to a lesser degree, cocaine, it had no impact on a LiCl-induced CTA. Since these data are somewhat parallel with those obtained in rats with bilateral lesions of the gustatory thalamus, further study is required to identify the specific contribution of these two nuclei to this phenomenon. Supported by DA 09815, DA 12473, and DA 017416-01.

Lower fasting and postprandial ghrelin levels in obese binge eaters. A. GELIEBTER, E.K. YAHAV, M.E. GLUCK, S.A. HASHIM. *NY Obesity Research Center, Departments of Medicine and Psychiatry, St. Luke's-Roosevelt Hospital Center, Columbia University College of Physicians and Surgeons, NY.*

Binge-eating disorder (BED), characterized by ingestion of binge meals without purging afterwards, is found in a sizable subset of obese individuals. The purpose of the study was to ascertain possible abnormalities in hormones influencing appetite in BED, especially ghrelin, an orexigenic peptide, which was expected to be elevated. Measurements were made of plasma insulin, leptin, glucagon, cholecystokinin (CCK), and ghrelin, as well as glucose, prior to and after 5 min ingestion of a nutritionally complete liquid meal 300 kcal (418 kJ), at −15, 0, 5, 15, 30, 60, 90, 120 min. An acetaminophen tracer was used to assess gastric emptying rate. Appetite ratings including fullness were also obtained. Three groups of comparably overweight and obese women (body mass index [BMI] = 35.1 ± 5.0 SD; percentage body fat by air displacement = 44.9 ± 4.7 SD) participated: 11 BED, 14 BE (subthreshold BED), and 12 non-binge eating normals. Contrary to the hypothesis, the BED subjects, compared to the normals, had lower fasting ghrelin concentrations prior to the meal, a lower area under the curve (AUC), and a smaller decline in ghrelin post-meal (all P values <0.05). None of the other blood values differed significantly between groups, including acetaminophen, reflecting gastric emptying rate, nor did ratings of fullness. After the BED subjects were treated ($n = 5$) or wait-listed ($n = 4$), baseline ghrelin ($P = 0.01$) and AUC ghrelin increased ($P = 0.02$), across both intervention groups, in which most subjects 7/9 remitted and stopped binge eating. Although unexpected, the lower fasting and post-meal plasma ghrelin in BED is consistent with lower ghrelin in obese than in lean individuals, and suggests down regulation by overeating. Supported by NIH DK54318 (AG).

How young children use emotion information from others to make decisions about novel food. M. GOLDSMITH, D. MUMME, R. KANAREK. *Tufts University, Medford, MA, USA.*

Young children are frequently exposed to novel foods from the media and environment, but what information do children find important? We examined kindergarten children's reactions to novel food after watching a video of a mother and peer model eating or not eating a novel food. If a model tasted the food, the reaction was either positive or negative. The models' emotion reactions to the novel food varied, including liking, disliking or disgust with refusing to eat. The participating child watched a set of mother/peer reactions to one novel food, and then was offered the same novel food to taste. This was repeated twice with two other foods. The results showed that children always tasted the novel food except when both models refused to eat the food. The emotion messages did not significantly effect the children's Likert ratings of the novel foods. Asking about the children's willingness to eat the food again later provided insight into what they might do after the experimental session. For a preferred novel food, the emotion messages did not influence the children's future eating behavior, but for a nonpreferred novel food the emotion messages had a slight influence. The model who gave the emotion message was important to the children. Overall, the peer was more influential than the mother. When the models gave different messages, children were influenced by the model who gave more positive messages than negative messages. In summary, kindergarten children are accepting of novel food to taste and other's positive reactions are more important than negative messages. Other people's disgust reaction to novel food does not deter children from eating novel food.

Low CCK-8 doses sensitized gastric mechanoreceptors to dynamic distension in pigs. W.L. GROVUM, W.W. BIGNELL, B.R. ELLISON. *Department of Biomedical Sciences, Ontario Veterinary College, University of Guelph, Ontario, Canada N1G 2W1.*

The physiological significance of cholecystokinin as a satiety signal was investigated. Yorkshire pigs (22; 29 to 64 kg) were fasted overnight with water available and anesthetized with sodium pentobarbital. They were prepared surgically to compare the threshold doses of CCK-8 required i.v. to (a) evoke pancreatic secretion (cannulated pancreatic duct; counted drops), (b) tonically contract the gallbladder (incised apex; replaced bile with fluid filled sac; measured pressure), (c) evoke duodenal contractions (inserted fluid filled sac into lower duodenum; measured pressure), (d) excite slowly adapting gastric mechanoreceptors sensing distension (recorded impulses/sec in single afferent vagal fibers while air pressures in a plastic bag in the stomach were increased from 0 to 19 mmHg and back to 0 over 10 to 33 s) and (e) depress food intake (values for pigs taken from literature). Parameters (a) to (c) in 4 pigs were all increased by 0.03 μg CCK-8/kg. In (d) involving 10 receptors from 7 pigs (36–57 kg), neural activity was increased by 0.06 μg CCK-8/kg (lowest dose tested) in 5 receptors, by 0.25 μg/kg in 2 receptors and by 1 and 4 μg/kg in 2 others. One unit failed to respond to CCK. In (e), anorexic effects were apparent at 0.44 and 0.91 μg/kg with pigs fasted 4 and 23 h respectively. The hunger thus generated may have inadvertently raised the thresholds considerably. If more sensitive testing decreases the threshold for anorexia and if the afferent activity produced by the receptors tested contributes to 'fullness', its seems possible in a majority of pigs that CCK may be a physiological signal of satiety.

Assessment of gastric compliance response to a meal: gastric sensory motor function in patients with *Bulimia nervosa* (BN). J.L. Guss, H.R. Kissileff, E. Zimmerli, M.J. Devlin, B.T. Walsh. *Obesity Research Center, St Luke's-Roosevelt Hospital-Columbia University. New York, NY 10025, USA.*

In laboratory binge meals, patients with BN eat substantially more than do normal individuals. Nevertheless, patient and control subjects reach similar levels of fullness by the end of their meals, which suggests that BN patients have impaired sensitivity to the filling effects of large meals. Likewise, BN patients have impaired gastrointestinal responses to meals, including diminished gastric-emptying, CCK-release and gastric-relaxation response. The aim of this study was to determine whether meal-induced changes in sensory and motor responses to gastric distension (i.e. gastric compliance, the change in gastric volume as a function of changing pressure) differ between BN patients and healthy controls. BN patients ($N = 16$) and healthy controls ($N = 13$) each rated the intensity of various sensations at increasing pressure-increments of 2-mmHg, until gastric volume reached 750-ml or the subject reported pain. Pressure was increased every 2-min by means of a Barostat. The procedure took place before and after subjects consumed Ensure (200-ml; 1 kcal/g). Gastric compliance increased significantly ($P < 0.0001$) but similarly for both patients and controls in response to the meal [preprandial (ml/mmHg): controls, 51.9 ± 5.63 SE; patients, 47.8 ± 4.11 SE; postprandial: controls, 67.1 ± 6.49 SE; patients, 65.6 ± 4.97 SE]. Ratings of fullness and other sensations during the test did not differ between groups. Thus, gastric-compliance responses to a meal, and corresponding sensitivity to gastric distension, appeared normal among BN patients under our test conditions. However, further research is warranted in order to elucidate the interconnections between disturbed gastric function and the sensory and behavioral satiety deficits in BN. Supported by MH12901, MH42206 and NYORC.

Effects of chronic intracerebroventricular (ICV) infusion of leptin and insulin on motor-activation induced by d-amphetamine in rats. J. Hao, S. Cabeza De Vaca, K. Carr. *Departments of Psychiatry and Pharmacology, New York University School of Medicine, New York.*

Recently, attention has turned to the possibility that the endocrine adiposity hormones insulin and leptin may regulate appetitively motivated behavior, in part, by modulating brain dopamine function. It has been hypothesized that the increased behavioral sensitivity to psychostimulant challenge in chronically food-restricted rats may be triggered by the accompanying hypoinsulinemia or hypoleptinemia. The purpose of the present study was to determine whether 12–14 days of ICV infusion of insulin or leptin alters the motor-activating effect of d-amphetamine in ad libitum fed or food-restricted rats. Third ventricular infusion of insulin (5 mU/day) produced a trend toward decreased amphetamine-induced locomotion in ad libitum fed rats tested days 5–7 and 10–12 of infusion. However, in a second experiment, insulin (10 mU/day) had no effect on behavioral sensitivity to amphetamine. In food-restricted rats, maintained at 80% of pre-restriction body weight, insulin infusion (5 mU/day) again had no effect on behavioral sensitivity to amphetamine. Lateral ventricular leptin infusion (12 mg/day) produced a significant decrease in food intake and body weight in ad libitum fed rats, and augmented the locomotor response to amphetamine. 8–10 days after cessation of infusion, body weights and amphetamine sensitivity had returned to control levels. In food-restricted rats, leptin infusion produced no further alteration of intake or body weight and failed to alter the locomotor response to amphetamine. These results suggest that leptin augments behavioral sensitivity to amphetamine in ad libitum fed rats secondary to its effect on body weight, and that neither hypoleptinemia nor hypoinsulinemia may play an important role in the augmentation of psychostimulant sensitivity in food-restricted rats. Supported by 5F30DA16158-02 (J.H.).

CCK and 5-HT interact to enhance suppression of food intake-involvement of 5-HT3 receptors. M.R. HAYES, M. COVASA. *Department of Nutritional Sciences, College of Health and Human Development, The Pennsylvania State University, University Park, PA, 16802.*

We have previously shown that serotonin type-3 receptors (5-HT3R) participate in cholecystokinin (CCK)-induced suppression of food intake. To further examine the relationship between the cholecystokinergic and serotonergic systems in the short-term control of food intake we examined the following: (1) participation of 5-HT3R in 5HT-induced suppression of sucrose intake; (2) the interaction between CCK and 5HT in suppression of food intake. In the first study, food deprived rats received ondansetron (1.0, 0.5, 0.25, 0.125 mg/kg, IP), a highly selective 5-HT3R antagonist prior to 5-HT administration. At all doses, administration of ondansetron alone did not alter 30-min intake of 15% sucrose compared to control. Administration of 5-HT (1.0, 0.5, 0.25 mg/kg, IP) reduced 30-min sucrose intake (35.0, 18.9, and 18.4%, respectively) compared to saline. Pre-treatment with ondansetron (1.0 mg/kg) significantly attenuated 5-HT (1.0 mg/kg)-induced suppression of intake by 50.8%. In a separate experiment, we examined the anorectic effect of simultaneous CCK and 5-HT administration on sucrose intake. Both CCK (0.5 μg/kg, IP) and 5-HT (0.5 mg/kg, IP) significantly reduced 20-min intake by 35.4 and 35.7%, respectively, compared to control. CCK and 5-HT administered together resulted in an additional 15% suppression, accounting for an overall 50.7% reduction in sucrose intake compared to saline. These studies confirm and extend previous work indicating that peripheral administration of 5-HT suppresses food intake by acting at 5-HT3R. In addition, these studies show that 5-HT and CCK interact to produce an enhancement in the suppression of food intake.

Mechanisms of increasing meal size—the influence of distraction. M.M. HETHERINGTON. *School of Psychology, University of Liverpool, Liverpool, England.*

Eating in humans typically occurs in anticipation of energy requirements, therefore, external cues are of primary importance in determining when, how much and what foods to eat. A potent environmental factor promoting meal size is the presence of familiar others. Many studies have demonstrated social facilitation effects of between 40% and 70%. It has been suggested that social facilitation occurs simply as a function of the time spent around food. Three recent studies conducted in our laboratory have explored distraction as a possible mechanism underlying social facilitation of eating. In addition, we have compared the impact on meal size of different types of distractions including audiovisual and taste distractors. This presentation will focus on the effect of competing tasks on meal size in different eating contexts (eating with others, eating alone) and amongst different types of consumers (external eaters, restrained eaters). Overall, it will be argued that distraction draws attention away from direct controls which normally accompany satiation, including sensory-specific satiety, thereby extending the time taken to consume the meal and promoting a larger meal size. Research funded by a LINK grant from the ESRC and Slimming World.

Memory for recent eating and its effects on appetite. S. HIGGS. *School of Psychology, University of Birmingham, Edgbaston, Birmingham, B15 2TT, UK.*

Many current models of appetite control acknowledge that meal size in humans is likely to be the outcome of a complex interplay between both physiological and non-physiological factors. Thus, although there is little argument that food intake is related to nutritional status, it is also the case that both social and cognitive factors have a profound effect on eating behaviour. Work in our laboratory has suggested that one cognitive factor that may have an important role to play in control of appetite is memory for what has been recently consumed. We have shown that reminding participants of a lunchtime meal suppresses intake at a taste test later in the afternoon. This effect is specific to recalling food eaten that day, since asking participants to think about lunch consumed the previous day had no effect. This presentation will explore the conditions under which memory for recent eating influences intake. The effect of the perceived energy of the recalled meal, the influence of palatability on the memory effect, and the relationship between appetite ratings and strength of subsequent recall will be discussed. These studies, along with reports from other labs of multiple meal eating in amnesic patients, suggest that merely remembering that one has eaten recently is sufficient to alter food intake and that memory may have a role to play in controlling everyday eating.

Leptin treatment in activity-based anorexia. J.J.G. HILLEBRAND, M.P. KOENERS, A.J. SCHEURINK, G. VAN DIJK, M.J.H. KAS, R.A.H. ADAN. *Department of Pharmacology and Anatomy, Rudolf Magnus Institute of Neuroscience, UMC Utrecht. Universiteitsweg 100, 3584 CG Utrecht, The Netherlands.*

Activity-based anorexia (ABA) is an animal model for anorexia nervosa, which models hypophagia and hyperactivity. In ABA rats are food restricted (1 h food access per day) and have access to a running wheel. The combination of these two factors leads to a fast and severe body weight loss; rats eat even less than is possible in 1 h while running wheel activity is increased. We hypothesize that ABA is caused by decreased leptin signaling as a consequence of starvation. Indeed, it has been shown before that leptin treatment of starved rats decreased hyperactivity in a semi-starvation induced hyperactivity model (SIH) (Exner et al, 2000). In the study described here, we further investigated the role of leptin in the ABA model. Rats were chronically infused (5 days) with 4 μg leptin per day (or saline) into the lateral ventricle. ICV infusion of leptin in the ABA model resulted in practically absence of running wheel activity in the dark phase ($P = 0.001$) and light phase ($P = 0.001$). As well leptin treatment further decreased food intake ($P = 0.000$). Leptin treatment did not improve physical condition of rats exposed to the ABA model, but in fact, decreased survival of rats in the ABA model. The beneficial effect of decreased energy expenditure (running activity) following leptin treatment was counterbalanced by hypophagia. We hypothesize that leptin also influences other aspects of energy expenditure, e.g. metabolic rate, which might contribute to a decreased survival in the ABA model. We conclude that leptin treatment decreases survival in ABA and is therefore not recommended as pharmacotherapy in anorexia nervosa patients.

Estradiol affects synaptic input of POMC cells in reducing food intake and adiposity. H.L. HORVATH, Q. GAO, G. MEZEI, S. DIANO. *Department of Obstetrics, Gynecology and Reproductive Sciences* and Department of Neurobiology#, Yale University School of Medicine, New Haven, CT 06520.*

We have recently uncovered that leptin rapidly re-arranges the synaptic input of hypothalamic arcuate nucleus feeding circuits resulting in increased pro-opiomelanocortin (POMC) tone followed by decreased food intake and adiposity. The gonadal steroid, estradiol, also reduces appetite and adiposity and influences synaptic plasticity. We revealed that estradiol triggers a robust increase in the number of excitatory, glutamate inputs of arcuate nucleus POMC neurons in wild type animals. This re-arrangement of synapses in the arcuate nucleus is leptin-independent since it was also evident in leptin- (ob/ob) and leptin receptor deficient (db/db) mice and was paralleled with decreased food intake and increased energy expenditure in these mutant, obese animals. These observations further support the notion that synaptic plasticity of arcuate nucleus feeding circuits is a critical element in body weight regulation and offer alternative approaches to reduce adiposity during failed leptin signaling.

Weight gain during supervised drug abstinence: Does food compete for brain reward? C.C. HODGKINS, K. FROST-PINEDA, M.S. GOLD. *Gateway Community Services (CCH) and University of Florida (KFP and MSG).*

Adolescent obesity and substance abuse pose a serious public health problem in the United States. Both problems are related. The relationship between eating behavior and substance abuse is increasingly recognized among addiction researchers. Recent studies on adolescent addicts in residential treatment illustrate significant weight gain and increase in Body Mass Index (BMI) during supervised and confirmed abstinence from drugs and alcohol. The purpose of this study was to examine whether there is a relationship between adolescents' primary drugs of abuse and their weight/BMI at admission to treatment and 60 days into their treatment episode. Both pre and post weight and Body Mass Index (BMI) were used as outcome variables. 120 adolescent males randomly assigned to aerobic exercise only or aerobic exercise plus nutrition education including a food-mood diary and compared with treatment-as-usual (TAU). Primary drugs of abuse were categorized into marijuana, alcohol, and poly-substance abuse. The research hypotheses were addressed through a repeated measures analysis of within-subjects and between-subjects effects. The results of the study suggest that this male adolescent sample experienced significant weight gain and BMI increase regardless of primary drug of abuse or treatment intervention. These findings support our work and other research that weight gain is associated with drug use cessation. Eating can compete with drugs and alcohol for brain reward.

Daily sugar bingeing enhances accumbens dopamine release repeatedly, like a drug of abuse, and sham bingeing eliminates the acetylcholine satiety signal. B.G. HOEBEL, N.M. AVENA, P. RADA. *Department of Psychology, Princeton University, Princeton, NJ 08544, USA.*

Intermittent fasting and bingeing on sugar (10% sucrose) can lead to signs of addiction in rats, including augmented intake, changes in mu and dopamine (DA) receptor binding, behavioral cross-sensitization to amphetamine, naloxone-induced withdrawal, and augmented reinstatement after abstinence. Most drugs of abuse increase extracellular DA in the accumbens repeatedly. Palatable food also releases DA, but the effect wanes during a long meal and disappears with repetition. In Exp. 1, rats were maintained on a diet of 12-h daily access to sugar and chow for 21 days to acquire a binge pattern of eating. Controls had access to sugar only for 1 h on Days 1 and 21. After 3 weeks, sugar intake in the bingeing rats increased extracellular DA in the accumbens shell to 130% of baseline, analogous to a low dose of a drug of abuse. Extracellular ACh increased to 133% at the end of the sucrose meal, confirming a role for ACh in satiety signaling. In Exp. 2, rats on the same intermittent schedule ate with a gastric fistula open for the first hour of access each day (sham-feeding). DA was again released repeatedly, but acetylcholine did not increase in spite of larger than normal meals (55 ml vs. 18 ml). Taste alone is sufficient to release DA repeatedly in sugar-dependent animals, and purging eliminates the ACh satiety signal. Thus, intermittent bingeing on sweet food can act in the brain like a drug of abuse, and DA sensitization and opioid dependency may contribute to bulimia nervosa. Supported by USPHS grants DA-10608 and MH65024.

Satiation of thirst associated with the inhibition of gastric emptying of ingested fluids. M.L. HOFFMANN, E.M. STRICKER. *Department of Neuroscience, University of Pittsburgh, Pittsburgh, PA 15260, USA.*

Rats were deprived of drinking water (but not food) overnight. When given water again, rats drank almost continuously before pausing to groom. The amount of ingested water in the stomach of each animal, plotted as a function of the amount consumed, indicated that initially water emptied virtually as fast as it was consumed, but after a few minutes of drinking gastric emptying stopped and the stomach began to fill; at this time plasma Na + (pNa) had not yet begun to fall, but inhibition of vasopressin (VP) secretion was evident. Nonetheless, water intake continued. When drinking ended soon thereafter, 6–8 ml were found in the stomach. Other dehydrated rats drank 0.15 M NaCl instead of water and consumed larger amounts. Most animals emptied virtually all ingested fluid for 3–5 min before gastric emptying stopped, at which time pNa and VP secretion were not altered. When drinking ended a few minutes later, 6–8 ml again were found in the stomach. A third group of dehydrated rats was given 0.20 M NaCl to drink, and the distribution of values when gastric fill was plotted as a function of intake was similar to that observed when rats drank water. These results suggest that gastric emptying ceases soon after drinking starts (when water or hypertonic saline is consumed), presumably because of the visceral detection of osmotic dilution or concentration, or somewhat later (when isotonic saline is consumed), presumably because intestinal stretch ultimately becomes large enough to terminate gastric emptying. The termination of fluid intake by thirsty rats occurs a few minutes after gastric emptying stops, when gastric fill generates a signal that inhibits further intake.

Effects of peanut oil consumption on appetite and food choice. S.S. IYER, L.A. BOATENG, R. LOPES, P. LOKKO, J.B.R. MONTEIRO, R.D. MATTES. *Department of Foods and Nutrition, Purdue University, IN 47907, USA; Food Research Institute, M.20 Accra, Ghana; Universidade Federal de Viscosa, Viscosa, Brazil.*

Peanuts have a high satiety value. The role of its lipid fraction in promoting satiety is not clear. We studied the effects of chronic peanut oil consumption on appetite and food choice. One hundred and twenty nine, healthy adults from three countries (Brazil, Ghana and United States) were randomly assigned to one of four treatment arms: consumption of 470 kcal peanut oil, olive oil or safflower oil for 8 weeks or no dietary intervention. Participants received no dietary guidance. They completed subjective appetite questionnaires eliciting information about hunger, fullness, desire to eat, and prospective consumption during all waking hours for 1 or 3 days at weeks 0, 2, 4, 6 and 8. Diet records were completed at weeks 0, 4 and 8. No difference in appetitive ratings was observed over time within any treatment or between treatments. Total caloric intake was significantly higher at week 8 relative to baseline ($F = 10.08$, $P < 0.05$). Differences were: peanut oil—$197 + 114$; olive oil—$237 + 121$; safflower oil—$274 + 90$; control—$75 + 71$. There were no significant differences across countries in appetite ratings or dietary compensation. These data suggest that components other than the lipid fraction in peanuts play a role in promoting satiety.

Dexamethasone decreases food intake and body weight, increases serotonin turnover in the brain. J.W. JAHNG, N.Y. KIM, G.T. KIM, J.Y. LEE, H.J. CHO, D.G. KIM, H.T. KIM. *Department of Pharmacology, BK21 Project for Medical Science, Yonsei University College of Medicine, Seoul 120-752, Korea; Department of Psychology, Korea University, Seoul 136-701, Korea.*

Stress has a major impact on feeding behavior. Plasma glucocorticoids and the hypothalamic monoamine release sensitively respond to stress and feeding. We examined the effects of dexamethasone (DEX), synthetic glucocorticoid, on brain serotonin and norepinephrine levels as well as on feeding behavior. Male Sprague–Dawley rats (250–300 g) received 4 daily injections of subcutaneous DEX (0, 0.1 or 1.0 mg/kg). The control group (0 mg/kg DEX) received only saline. Daily injections were given at 5:00 PM, i.e. 2 h before the onset of dark period. Amount of food consumed between 7:00 PM and 9:00 PM of the first injection day (day 1) was not different among the groups. A suppressive effect of DEX on feeding was found on day 2 in a dose-dependent manner, and sustained until day 5. Body weight gain did not alter until day 2, however, significantly decreased by either doses of DEX on day 3, and the decrease became bigger with repeated treatment of DEX in a dose-dependent manner. For HPLC analysis of brain serotonin and norepinephrine contents. rats were sacrificed 24 h after the last DEX. DEX dose-dependently decreased serotonin levels, but increased its metabolite, 5-HIAA, both in the hypothalamus and mid-brain raphe. Norepinephrine content was slightly increased by high dose DEX in the mid-brain, but no effect in the hypothalamus. These results indicate that DEX does not acutely affect either food intake or body weight gain, and suggest that a chronic suppressive effect of DEX on feeding behavior may correlate with the decreases in brain serotonin levels, which likely due to its increased turnover rate.

Dexamethasone modulates brain monoamine levels and feeding differentially in pre-pubertal and pubertal female rats. J.W. JAHNG, H.J. CHO, G.T. KIM, S.H. CHOI, N.Y. KIM, D.G. KIM, N.D. GEARY. *Department of Pharmacology, BK21 Project for Medical Science, Yonsei University College of Medicine, Seoul, 120-752, Korea; Department of Psychiatry, Weill Medical College of Cornell University, White Plains, NY 10605.*

We investigated the effects of glucocorticoids, a stress hormone, on brain monoamine levels and feeding behavior in pre-pubertal and pubertal female rats, respectively. Nulliparous female Sprague–Dawley rats were mated with proven breeder male in our laboratory. Female pups were single caged after weaning, received daily injection of subcutaneous DEX (0, 0.1 or 1.0 mg/kg) on PND 28 and 29 (pre-pubertal period), or on PND 38 and 39 (pubertal period). The control groups (0 mg/kg DEX) received saline at each injection. DEX at high dose suppressed food intake of the pre-pubertal group, however, not of the pubertal. DEX induced body weight loss in a dose-dependent manner in both groups. Rats were decapitated 24 h after the second DEX, brain levels of norepinephrine (NE), serotonin (5-HT) and its metabolite, 5-HIAA, were determined by HPLC with the hypothalamic and mid-brain tissues. In the pre-pubertal rats, DEX increased 5-HT and NE, decreased 5-HIAA level of the mid-brain, and decreased 5-HT and 5-HIAA, did not change NE level of the hypothalamus. However, in the pubertal rats, DEX decreased 5-HT and 5-HIAA, increased NE level of the mid-brain, and decreased 5-HT, increased 5-HIAA and NE levels of the hypothalamus. A dose effect of DEX was found in most of the HPLC measurements. These results suggest that feeding response to stress may change by the onset of puberty in female, and this change may correlate with the differential regulation of glucocorticoids on brain 5-HT and NE systems before and after the onset of puberty. Supported by KISTEP (JWJ).

Effect of restraint stress on the adrenal steroidogenesis of mouse fed with high salt diet. J.W. JAHNG[a], B. SHIN[b], Y.W. MOON[b]. [a]*Department of Pharmacology, BK21 Project for Medical Science, Yonsei University College of Medicine, Seoul, 120-752, Korea;* [b]*Department of Biology, Catholic University College of Medicine, Seoul, 137-701, Korea.*

We previously reported that the adrenocortical expression of cytochrome P450 11β-hydroxylase and the plasma corticosterone levels are concomitantly increased by 4 weeks of high salt diet (HSD) in mice. This result suggested that HSD may chronically increase the adrenal steroidogenic activity of the subjects. Since the plasma corticosterone level is known to respond sensitively to stress, we examined if restraint stress produces a synergic effect on the adrenal steroidogenic activity of the HSD mice. Mice had ad libitum access to 3% sodium chloride as the only drinking fluid (HSD) for 4 weeks. The control mice received free access to tap water instead. Half of mice in each group were subjected to restraint stress, i.e. taping all the limbs, for 2 h at the end session of HSD diet, and the rest untouched. Mice were transcardially perfused with 4% of paraformaldehyde, the adrenal glands rapidly dissected for P450 immunohistochemistry. Cardiac bloods were collected for the plasma corticosterone assay. Food intake was decreased initially, but returned to the control level by 1 week of HSD, however, the body weight gain consistently suppressed by HSD. Plasma corticosterone level was markedly increased either by HSD or restraint. Interestingly, restraint stress suppressed the HSD-induced increase of the plasma corticosterone. The adrenocortical expressions of P450 11β-hydroxylase, a major regulatory enzyme of corticosterone biosynthesis, were analyzed in each group of mice by immunohistochemistry.

Reactivity to smoking cues in dietary restrained smokers in the presence and absence of food cues. R. JENKS, S. HIGGS. *School of Psychology, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK.*

One of the primary motivations for smoking in restrained eaters is weight control. If smoking in restrained eaters is more frequently associated with food or thoughts of food, then reactivity to smoking related cues should be enhanced in the presence of food in this population compared with unrestrained eaters. Nineteen female undergraduates attended two sessions (food present and food absent), following minimum cigarette deprivation. At each session, participants were presented with a cigarette and neutral cue in a counterbalanced order. Pre and post cue measures included the brief version of the Questionnaire for Smoking Urges, and physiological and subjective measures of arousal. For restrained participants there was a larger increase in cigarette craving in the presence of food compared with the unrestrained participants. In addition, the presence of food was associated with a significantly larger increase in heart rate in restrained eaters. Subjective arousal ratings were not significantly affected by either cue type or session. Both craving and physiological measures are consistent with the hypothesis that restrained eaters form an association between smoking and eating, which can result in enhanced cigarette craving in the presence of food.

Ethanol intake is increased by 3rd ventricle or PVN galanin injection and reduced by a GAL antagonist. D.F. JOHNSON[a], M.J. LEWIS[a], P. RADA[a,b], N.M. AVENA[a], S.F. LEIBOWITZ[c], B.G. HOEBEL[a]. [a]*Department of Psychology, Princeton University, Princeton, New Jersey 08544, USA;* [b]*Laboratory of Behavioral Physiology, University of Los Andes, Merida, Venezuela;* [c]*Laboratory of Behavioral Neurobiology, The Rockefeller University, New York, NY 10021, USA.*

Ethanol intake stimulates galanin (GAL) expression in several hypothalamic sites, including the paraventricular nucleus (PVN), a site where GAL stimulates food intake. We asked whether GAL also stimulates ethanol intake. In Exp. 1, rats had access to 7% ethanol and water for 12 h/day starting 4 h into the dark. Compared to vehicle, GAL (1.0 and 3.0 nM) infused in the 3rd ventricle increased ethanol intake during the light portion of the light cycle. During the dark, the GAL effect was smaller, but still significant. Microinjection of M40, a nonselective GAL receptor antagonist, blocked the GAL effect. In Exp. 2, rats with ad libitum access to 4% ethanol for 4 weeks were designated 'high drinkers' (>1.5 g/kg/day) or 'low drinkers' (<1.0 g/kg/day). GAL (0.5 and 1.0 nM) infused unilaterally into the PVN dose-dependently increased ethanol intake in high drinkers. This increase was not observed when GAL was infused 2 mm dorsal to the PVN. Microinjection M40 (0.5 nM) decreased ethanol intake. Thus, both 3rd ventricular and PVN injection of GAL, at doses known to induce feeding, acted via a GAL receptor to potentiate ethanol intake in rats that drink alcohol at moderate levels. Because ethanol itself can increase expression of GAL mRNA in the PVN, this could set the stage for a positive feedback loop between hypothalamic GAL and ethanol intake that may have a role in alcohol dependence. Supported by: USPHS grants AA012882 and AA014074.

Fructose-sweetened beverages promote adiposity in mice. H.S. JÜRGENS[#], W. HAASS, C. THÖNE-REINEKE, T.R. CASTAÑEDA, J. SPRANGER, M. RISTOW, H.-G. JOOST, P.J. HAVEL, M.H. TSCHÖP. *German Institute of Human Nutrition, Potsdam-Rehbrücke, Germany; Genome Research Institute, University of Cincinnati, Cincinnati, OH; University of California, Davis, CA.*

The recent obesity epidemic has been accompanied by an increase in *per capita* intake of dietary fructose, in large part due to increased consumption of soft drinks sweetened with high fructose corn-syrup or sucrose.

We investigated the effects of fructose and soft drink consumption in male NMRI mice ($n = 9$ per group, 3 months old). The animals had ad libitum access to standard chow, and to either (T1) water, (T2) water with fructose (15%), (T3) a sucrose-sweetened soft drink (10%) or (T4) a diet soft drink with aspartame for 63 days. Body weight increased in all four groups; but compared to T1 significantly only in T2 (+20.8%, from 39.7 0.7 to 47.9 1.4 g, $P = 0.003$). Changes in body fat mass (by NMR) were larger in T2 (+135.6%), T3 (+94.8%) or T4 (+99.8%) compared to T1 (+62.8%). In T2 body fat increased significantly within the study when compared to T1 ($P = 0.02$). There were slight, but not significant differences between the four groups regarding the total caloric intake (beverage + chow). Energy expenditure did not differ significantly between the study groups during treatment with fructose/soft drinks.

In summary, ad libitum access to fructose significantly increases body weight and body fat in mice. Surprisingly, metabolic changes rather than increased caloric intake or energy expenditure appear to represent the primary mechanism contributing to body fat gain. Based of these data, the metabolic effects of fructose, sucrose, aspartame, and their effects on energy balance and body adiposity deserve further study.

Reduced thermogenesis in New-Zealand obese (NZO) mice. H.S. JÜRGENS[a], S. ORTMANN[a], S. KLAUS[a], R. KLUGE[a], C. THÖNE-REINEKE[a], T.R. CASTAÑEDA[b], A. SCHÜRMANN[a], H.-G. JOOST[a], M.H. TSCHÖP[a,b]. *[a]German Institute of Human Nutrition, Potsdam-Rehbrücke, Germany; [b]Genome Research Institute, University of Cincinnati, Cincinnati, OH.*

Obesity results from a chronic imbalance between energy intake and energy expenditure, and is a serious health problem in industrialized countries.

Aim of this study was to dissect all major determining factors of energy balance and their possible malfunction in young NZO-mice, New-Zealand Black (NZB) and C57BL/6 (B6) before the NZO-mice develop obesity and diabetes. Body weight, body composition and food intake of five male NZO-, NZB- and B6-mice was monitored (starting age 5 weeks). Furthermore, we determined the thermal neutral zone (TNZ), respiratory quotient (RQ), total energy expenditure (TEE) and core body temperature as well as spontaneous physical activity.

In comparison to the B6-mice, the core body temperature in a 24 h average of the NZO-mice was approximately 1 °C lower (NZO: 36.68 ± 0.19 °C, B6: 37.61 ± 0.30 °C, $P < 0.05$). A decreased TEE per g body weight at 22 °C for the NZO-mice reflects a reduced thermogenesis ($P = 0.02$, NZO: 1.51 ± 0.04 kJ d^{-1} g^{-1}, B6: 1.69 ± 0.04 kJ d^{-1} g^{-1}). No significant difference in the RQ during the light phase was detected between the strains. However, during the active dark phase the RQ was significantly higher in NZO than in B6, suggesting increased lipogenesis and/or reduced lipid oxidation. Locomotor activity and caloric intake did not differ between the groups.

The results indicate that the obese phenotype of NZO is in part due to decreased thermogenesis and decreased energy expenditure, and that the strain exhibits a marked dysfunction of substrate utilization during the postprandial phase.

Role for ghrelin as an interoceptive discriminative cue. S.E. KANOSKI, E.A. WALLS, T.L. DAVIDSON. *Department of Psychological Sciences, Purdue University, West Lafayette, IN.*

The hyperphagic effects of ghrelin, an endogenous ligand for the growth hormone secretagogue receptor which is synthesized primarily in the stomach, are well documented. There is considerable evidence suggesting that systemic and centrally administered ghrelin increases food intake and body weight in rodents; however, the manner in which ghrelin produces these effects is still largely unknown. The purpose of this investigation was to determine if ghrelin has interoceptive sensory consequences similar to those produced by food deprivation. Rats ($n = 32$) were trained to use cues arising from 1 and 24-h food deprivation as discriminative signals for food (five sucrose pellets). One group (Group 24 +) received the pellets on training days following 24-h food deprivation, but not on training days following 1-h food deprivation. Group 1 + received the opposite contingency. Food magazine approach behavior served as the index of learning. After both groups showed asymptotic performance, generalization of discriminative responding to cues produced by intraperitoneal injections of either ghrelin (3 or 6 nmol) or saline was tested when the rats were 1-h food deprived. No sucrose pellets were presented during test sessions. The results showed group 24 + exhibited significantly more food cup approach behavior following ghrelin administration (6 nmol but not 3 nmol dose) than following saline, whereas Group 1 + showed the opposite pattern of responding. These findings indicate that systemic ghrelin produced interoceptive stimuli that generalized to interoceptive cues produced by 24-h food deprivation. This outcome suggests that ghrelin may influence food intake by producing an interoceptive 'hunger' signal. The effects of this signal can be dissociated from the potential effects of ghrelin on the postingestive and orosensory consequences of eating. NIH grant R01HD29792 (TLD) supported this research.

Effects of gastric evacuation on subsequent meals in ad libitum- and schedule-fed rats. J.M. KAPLAN, K.A. HAGUE, H.J. GRILL. *Department of Psychology, University of Pennsylvania, Philadelphia, Pennsylvania, USA.*

To explore gastrointestinal contributions to meal patterning, we measured the effects of evacuating the stomach on subsequent intake in rats feeding ad libitum during the dark phase, or maintained with three 60-min periods of food access (IMI = 3.5 h). In the ad libitum condition, 4.59 ($\pm$ 0.40) g of food (dry weight) was removed from the stomach via an indwelling cannula after 3.5 h of food access. The rats ($n = 12$) compensated for gastric evacuation within 30 min; intake was significantly elevated (relative to that under a mock-rinse control condition) by an amount (2.89 ± 1.12 g) not significantly different from the amount evacuated. The schedule-fed rats ($n = 9$) ingested a large meal within the first half of each of the three access periods, and distributed their daily intake roughly equally across meals. Gastric contents were removed at the end of the first access period, resulting in an accurate compensatory increase in the size of the second meal, initiated 3.5 h later; (dry weight withdrawn = 5.34 ± 0.76 g; intake increase relative to mock-rinse values = 5.03 ± 1.45 g, ns). The ad libitum-feeding experiment shows that the sizing of a given meal is sensitive to the amount remaining in the stomach from earlier meals. The schedule-feeding experiment goes further to argue that meal size is also sensitive to the amount that normally empties from the stomach during the inter-meal interval. In process is an evaluation of whether the rise in plasma ghrelin before a scheduled meal is modified by gastric evacuation. Supported by DK42284 and DK21397.

Brain imaging after recovery from anorexia and bulimia nervosa: New insights into serotonin and dopamine pathways contributing to eating disorders. W.H. KAYE, G.K. FRANK, U. BAILER, A. WAGNER. *Department of Psychiatry, University of Pittsburgh Medical Center, Pittsburgh, PA, USA.*

The brain pathways that are responsible for altered feeding behaviors, body image distortion, and anxious obsessive moods in individuals with anorexia nervosa (AN) and bulimia nervosa (BN) are not known. However several lines of evidence implicate serotonin and dopamine pathways. We have investigated women who were recovered from AN and BN (normal weight and menses, no pathological eating behavior, not on medications for >1 year). We hypothesize that vulnerabilities contributing to a risk for developing an eating disorder are present premorbidly and persist after recovery. Positron emission tomography (PET) with the radioligand [^{18}F]altanserin was used to assess binding of 5HT2A receptors and PET with [^{11}C]raclopride were used to assess binding of dopamine D2 receptors. We have studied 41 control women and 70 recovered subjects who were of similar age and weight. Recovered AN and BN women continued to have elevated anxiety, harm avoidance, and measures of obsessions, while novelty seeking was lower in AN compared to BN. Recovered AN and BN subjects had reduced 5HT2A receptor activity in cingulate regions, as well as alterations in regions that may be specific for subtypes. 5HT2A receptor activity was associated with measures of harm avoidance. Recovered AN subjects had altered activity of the Dopamine D2 receptor in subcortical regions. Considerable data suggest that serotonin and dopamine neuronal systems interact and contribute to the modulation of appetite and weight, mood, impulse control, and reward. These findings support the possibility that disturbances of serotonin and dopamine pathways contribute to the pathogenesis of eating disorders.

Neural systems recruited by drug- and food-related cues: studies of gene expression in prefrontal cortex. A.E. KELLEY, C. SCHILTZ, C.F. LANDRY. *Department of Psychiatry and Neuroscience Training Program, University of Wisconsin–Madison Medical School, 6001 Research Park Blvd., Madison, WI 53719.*

There is a growing realization that the neural pathways underlying motivation for food and those affected by drugs of abuse share many commonalities. Highly palatable food and rewarding drugs both stimulate specific neurotransmitter systems in cortico-striatal-hypothalamic circuits. Contextual cues associated with rewarding food or drugs can exert powerful effects on emotions and behavior, eliciting a motivational state of craving and 'wanting.' It is theorized that such cues can play an important role in relapse to drug use, and possibly also in non-homeostatic eating (food intake not driven by energy deficit). There is evidence that sensory cues associated with rewarding states activate prefrontal circuits, which may then engage subcortical brain regions controlling behavioral actions. We have recently investigated a model in rats where environmental cues are repeatedly paired with drug (morphine, nicotine) or food (chocolate, fat), and gene expression is analyzed in prefrontal cortex and other regions. Contextual cues associated with addictive drugs or palatable food cause increased expression of the transcription factors c-fos, NGFI-B, and Arc in prefrontal, ventral striatal, and certain hypothalamic areas. These genes may play important roles in the cellular plasticity associated with learned food or drug cravings. The PFC receives highly processed sensory input from amygdala and hippocampus, and influences motivational pathways through projections to nucleus accumbens and lateral hypothalamus. We propose that the potent effect that olfactory, gustatory, or visual stimuli can have on appetite may in part recruit prefrontal cortical circuits that drive downstream appetitive motivational systems. Supported by the National Institute on Drug Abuse.

Ketogenic and non-ketogenic high fat diets differentially affect the central melanocortin system. K.P. KINZIG[#], K.A. SCOTT, J. HYUN, T.H. MORAN. *Department of Psychiatry and Behavioral Sciences, Johns Hopkins University, Baltimore, MD.*

Diets low in carbohydrate, despite high fat content, are reported to result in weight loss in humans. While a small number of studies suggest that these diets are safe and effective in the short-term, studies examining the mechanisms by which ketogenic diets induce weight loss are sparse. To compare the effects of a ketogenic low-carbohydrate, high-fat diet (KD) to a diet high in fat and carbohydrate (HF), rats were given access one of 3 diets (chow (CH): 18.6% protein + 15.8% fat + 65.6% carbohydrate (3.4 kcal/g), KD: 19.9% protein + 75.1% fat + 5% carbohydrate (6 kcal/g), or HF: 15% protein + 60% fat + 25% carbohydrate (5.6 kcal/g)) for 7 weeks, with body weight and caloric intake measured daily. CH and KD rats gained weight at a similar rate and to a similar degree, while HF rats gained significantly more (227 ± 10.2 vs. 207.8 ± 12.8 vs. 313 ± 13.4 g). Daily caloric consumption was similar between CH and KD rats (107.1 ± 2.4 and 102.2 ± 0.9), whereas HF diet rats consumed significantly more (117.9 ± 1.4). After 7 weeks, KD rats had significantly more epididymal fat than HF diet rats, and both groups had more epididymal fat than CH rats. Expression of POMC mRNA in the arcuate nucleus and MC4 receptor (MC4R) mRNA in the paraventricular nucleus was measured by in situ hybridization. HF diet resulted in increased POMC and no change in MC4R expression, whereas KD resulted in decreased POMC and increased MC4R expression. These data demonstrate that maintenance on a low carbohydrate, high-fat diet results in alterations to the central melanocortin system.

Reversal of insulin resistance postpartum is linked to enhanced skeletal muscle insulin signaling. J.P. KIRWAN, M. JING, A. VARASTEHPOUR, L.PRESLEY, P.M. CATALANO, J.E. FRIEDMAN. *Department of Reproductive Biology, Case Western Reserve University; and Department of Pediatrics, Biochemistry and Molecular Genetics, University of Colorado Health Sciences Center, Denver, CO 80262.*

Insulin resistance is a well-described feature of late human pregnancy, and is a necessary metabolic adaptation that facilitates the provision of nutrients to the growing fetus. The present study describes the potential cellular mechanisms underlying the changes in insulin sensitivity in women from late pregnancy to postpartum. Nine non-obese women (Age, 32 ± 2 years; BMI, 21.2 ± 0.8) with normal glucose tolerance were studied during late pregnancy (30–36 weeks) and again ~1 year postpartum using a euglycemic–hyperinsulinemic clamp to determine insulin sensitivity. Vastus lateralis muscle biopsies were obtained in the basal state prior to each clamp. Insulin sensitivity improved 89% at 1 year postpartum, $P < 0.005$. Skeletal muscle insulin receptor (IR) protein increased 42% $P < 0.05$, however insulin stimulated IR tyrosine phosphorylation and IR tyrosine kinase activity were unchanged. IRS-1 expression increased 69% ($P = 0.05$) and the level of IRS-1 Ser312 phosphorylation (a negative regulator of insulin signaling) was significantly reduced by 50% from late pregnancy to post-partum. The change in insulin sensitivity correlated highly with the change in IRS1 protein ($r = 0.84$, $P < 0.007$) and inversely with IRS-1 Ser312 phosphorylation ($r = 0.79$, $P < 0.01$). In addition, the p85α regulatory subunit of phosphatidylinositol (PI) 3-kinase was markedly reduced by 55% ($P < 0.02$) postpartum. These findings suggest that changes in IRS-1 play a crucial role in the reversal of skeletal muscle insulin resistance one year postpartum, and suggest that a constitutive increase in IRS-1 Ser312 phosphorylation may be involved in triggering IRS-1 degradation, contributing to the insulin resistance phenotype of normal human pregnancy.

Ratings vs intake as measures of mechanisms of satiation in humans. H.R. KISSILEFF, J.L. GUSS, J.C. THORNTON, L. LEE, M. TORRES, C.M. ROQUE. *Obesity Research Center, St Luke's/Roosevelt Hospital, New York, NY 10025, USA.*

In order to study mechanisms, such as gastric distention, which inhibit food intake, amount eaten is usually measured, thereby confounding stimuli of the manipulation with stimuli produced by the test. This confounding could be prevented if ratings were used to indicate the compound stimuli that are equivalent to the intake at which a person feels satisfied and stops eating (i.e. 'optimal consumption'). This study was undertaken to determine whether ratings at optimal consumption could measure the effect of a manipulation as efficiently as intake. On two days of a four-day experiment, nine women and eight men were given two ad libitum yogurt shake meals, each after a 50-g or 640-g soup preload. On two other days subjects ate thirteen 75-g portions of shake. After each portion they rated how close they were to satisfaction with the amount eaten by marking in response to the question: 'how much have you eaten?' on a 150-mm line. The line was anchored at the ends by 'nothing at all' or 'so much I can't go on', and at the midpoint by 'just the right amount' or by 'amount that would usually satisfy'. 'Optimal consumption' was defined as the intake at the midpoint. After the 640-g, compared to the 50-g, preload in ad libitum meals, intakes were significantly reduced by a mean 119 g ± 36 SE ($t = 3.25$, $P = 0.006$). 'Optimal consumption' was reduced even more than intake (by 245 g ± 64 SE, $t = 3.8$, $P = 0.0022$) after the 640-g compared to the 50-g preload. Ratings at optimal consumption are as efficient as intakes for measuring satiation.

Use of artificially sweetened products in eating disorders. D.A. KLEIN, G.B. BOUDREAU, M.J. DEVLIN, B.T. WALSH. *Eating Disorder Research Clinic, Columbia University/New York State Psychiatric Institute, New York, NY.*

Use of low-calorie foods appears to be prevalent among persons with eating disorders. However, actual use patterns have not been quantified. The goal of this study was to examine the use of selected artificially sweetened products among women with eating disorders. Outpatients with Bulimia Nervosa (BN; $N = 36$), inpatients with Anorexia Nervosa (AN; $N = 20$), and non-eating disordered control women ($N = 24$) completed a survey to assess consumption of chewing gum, 'diet' beverages, and packets of artificial sweetener over the preceding 4 weeks. In general, similar proportions of women with and without eating disorders reported consuming each of these products. However, among those who endorsed consumption, significant group differences were present in amount consumed. Women with AN-binge/purge subtype reported the highest weekly consumption of 12-ounce servings of diet beverages (mean 72.1, ±65.5, vs controls: mean 9.7, ±8.3; $P < 0.001$ (for log-transformed data) and pieces of gum (32.3 ± 26.9; vs controls: 8.0 ± 11.3; $P = 0.010$); women with AN-restricting subtype reported greatest weekly consumption of sweetener packets (231 ± 264; vs controls: 7.94 ± 4.08; $P < 0.001$). These findings are consistent with hedonic preferences for sweet tastes previously measured in some studies in persons with AN and BN. This consumption of artificially sweetened products may be an index of appetitive drive in these populations.

Rapid changes of intracellular amino acid concentration in simulated anterior piriform cortex in response to amino acid deficiency. T.J. KOEHNLE, D.W. GIETZEN. *School of Veterinary Medicine: Department of Anatomy, Physiology, and Cell Biology, Univeristy of California, Davis, USA.*

Rats rapidly recognize amino acid deficient diets, taking on average just 15 min to reduce food intake and first meal duration. Prior research has shown that this prompt response is not dependent on taste or smell, and is correlated with the concentration of the dietary limiting amino acid in the anterior piriform cortex (APC). This report details the results of a discrete computer simulation of competitive amino acid transport by neurons in the APC. The model was implemented using published values for all parameters. Parameter values were varied over three orders of magnitude to determine the role of each model component. A combination of the System A transporter ATA1 and a sodium-independent neutral amino acid transporter was necessary and sufficient to account for data obtained from APC neurons in vitro. The model predicted a 30–76% depletion of intracellular threonine within 15 min of decreasing extracellular threonine concentration, depending on the assumptions used. The model also explains prior findings that extracellular threonine deficiency leads to increased intracellular concentration of other System A substrates. Results indicated that metabolism of other System A substrates must be increased to account for published values in vitro. The model also showed that increases in other amino acids outside the neurons would lead to transient changes in amino acid pools inside the neuron, potentially accounting for behavioral data obtained in vivo by injection of various amino acids into the APC. Increased intracellular concentrations of other amino acids by competitive exclusion of decreased extracellular threonine might be the initial signal causing detection of amino acid deficiency by neurons of the APC.

Experience-based plastic changes in nucleus tractus solitarius neurons in lysine-deficient rats. T. KONDOH[a,b], E. TABUCHI[a,c], H. NISHIJO[c], R. TAMURA[d], T. ONO[e], K. TORII[a,b]. *[a]Torii Nutrient-stasis Proj., ERATO, JRDC, Yokohama 221-0031; [b]Inst. Life Sci., Ajinomoto Co., Inc., Kawasaki 210-8681; [c]System Emot. Neurosi; [d]Integr. Neurosci.; [e]Mol. Integr. Emot. Neurosci., Toyama Med. Pharm. Univ., Toyama 930-0194, Japan.*

Preference for lysine increases in lysine-deficient animals. To understand the neural basis of preference changes during an essential amino acid deficiency, taste responses of nucleus tractus solitarius (NTS) neurons to the oral administration of five prototypical tastants (NaCl, sucrose, HCl, quinine HCl (QHCl), and monosodium glutamate), lysine·HCl and other amino acids were investigated in rats. Before starting neuronal recording, rats were housed for 7 days with free access to control diet (control group), lysine-deficient diet (lysine-deficient group), or lysine-deficient diet with free access to lysine solution (lysine-supplemented group). After the behavioral measurements, rats were anesthetized with pentobarbital. Taste solutions were delivered for 5 s in the whole oral cavity. Averaged neuronal responses to QHCl and arginine were reduced significantly both in lysine-deficient and lysine-supplemented groups compared to the controls. In contrast, significant increases in neuronal responses to sucrose and lysine. HCl were observed only in the lysine-supplemented group. In the multidimentional scaling, response to lysine. HCl was significantly correlated to the responses to HCl and QHCl in the control and lysine-deficient groups whereas lysine response was significant correlated to the responses to HCl and NaCl in the lysine-supplemented group. These results suggest that the NTS is one of the essential brain sites for the elevation of lysine preference in lysine-deficient animals, and the occurrence of plastic changes in NTS neuronal responses to the taste signals of deficient nutrient requires, at least in part, prior experience- or learning-based process to select the deficient nutrient.

The effects of rate-limited feeding on meal patterning, intake, and anticipation of limited daily access to alcohol solutions in HAD rats housed without time-of-day cues. A.E. KOSOBUD, G.V. REBEC, W. TIMBERLAKE. *Indiana University School of Medicine, Department of Neurology, Indianapolis, IN, 46202; Program in Neural Science, Center for the Integrative Analysis of Animal Behavior and Department of Psychology, Indiana University, Bloomington, IN 47405, USA.*

Rats given single daily injections of methamphetamine display increased locomotion during the period 1–3 h before the injection. This anticipation occurs in the absence of time-of-day cues and/or the SCN, and resembles the circadian anticipatory behavior that precedes meals. In the present study, 16 female HAD rats were housed singly in sound-isolated cages under constant dim light, and given 1 h access to 10% EtOH/water solutions at 24 h intervals. To test whether meals alter drug entrainment, 1/2 of the rats were restricted to eating rates of not more than 2 pellets (200 mg) every 5 min. The remaining rats were allowed food pellets ad lib. Anticipatory wheel running 1 h prior to alcohol access was enhanced in the rate-limited group relative to the free feeding group. Rate-limited and free feeding groups did not differ in daily pellets consumed, alcohol intake, body weight or wheel running. Rate-limited rats appeared to modify meal patterning by increasing the duration of meals, while preserving the number of meals/day and pellets consumed/meal. The results are consistent with our hypothesis that drugs of abuse share with food an ability to entrain anticipatory behavior, which may reflect an underlying shift in motivation to seek and take drugs. Supported by NIAAA (AA07611) and NIDA (DA11092 and DA02451).

Estrogen effects on AT1 receptors in the subforncial organ: an in situ hybridization study. E.G. KRAUSE[#], T.L. STINCIC, K.S. CURTIS, R.J. CONTRERAS. *Program in Neuroscience, Department of Psychology, Florida State University, Tallahassee, FL 32306.*

Recent studies from our laboratory show that estrogen replacement in ovariectomized (OVX) female rats decreased the water intake elicited by systemic injections of isoproterenol, a β-adrenergic agonist that stimulates water intake by activating the renin-angiotensin-system (RAS). Additionally, this difference is not due to estrogen mediated changes in plasma renin activity. Taken together, these observations suggest that estrogen attenuation of RAS-elicited water intake is centrally mediated. Consistent with this idea, subsequent studies revealed an estrogen-mediated decrease in brain activation after peripheral isoproterenol; specifically, Fos immunoreactivity (IR) in the subfornical organ was reduced in rats treated with estrogen. The subfornical organ (SFO) contains angiotensin type 1 receptors (AT1) which bind circulating angiotensin II and activate central pathways mediating water intake. Thus, we hypothesize that estrogen decreases AT1 receptor expression and may underlie both the attenuation of RAS elicited Fos IR and water intake. Therefore, the goal of this experiment was to determine whether estrogen treatment alters the mRNA expression of the AT1 receptor using in situ hybridization. Rats were OVX and 1 week later treated with estradiol benzoate (EB; 10 μg) or vehicle (OIL) for two consecutive days. Forty-eight hours after the second injection, rats were sacrificed and brains were removed and processed for in situ hybridization. Preliminary results show that rats treated with EB had reduced AT1 mRNA in the SFO (0.0233 ± 0.00498 optical density) compared to those treated with the OIL vehicle (0.048 ± 0.0106 optical density). These results support our hypothesis and suggest a mechanism for estrogen effects on RAS-induced water intake and the concomitant decrease in central activation. Supported by NIH DC04785 and DK063754-01.

Fra-2 expression in the amygdala is increased during conditioned taste aversion as measured by laser capture microdissection and in situ hybridisation. B.S. KWON[#], T.A. HOUPT. *Biological Sciences, Program in Neuroscience, Florida State University, Tallahassee, FL, USA.*

Conditioned taste aversion (CTA) learning occurs after the pairing of a novel taste with a toxin (e.g. sucrose with LiCl). c-Fos is necessary for CTA, but because c-Fos is induced by LiCl even in the absence of learning, c-Fos alone is not sufficient: the expression of other Fos- and Jun-family membersmay also be required. To screen the expression of the AP-1 transcription factors within small areas, RT-PCR analysis was used after laser capture microdissection (LCM) of the amygdala. In situ hybridization (ISH) was performed to confirm the RT-PCR results. Adult male rats were implanted with intraoral catheters. Rats were infused with 5% sucrose (6 ml/6 min) or injected with LiCl (12 ml/kg, 0.15 M, i.p.) or given sucrose paired with LiCl, or not treated ($n = 3$/group for LCM and 6/group for ISH); 1 h later their brains were dissected. The lateral, basolateral, and central subnuclei of the amgydala of single 5 μm sections from individual rats were dissected using the Arcturus PixCell II system. mRNA was extracted and RT-PCR performed. c-Fos mRNA was highly increased in the central amygdala after LiCl and sucrose/LiCl, but not other regions. Fra-2 mRNA increased in the basolateral and lateral amygdala after sucrose, and in the central amygdala after LiCl or sucrose/LiCl. There were no differences between groups in c-Jun, JunB, FosB, Fra-1, or ICER mRNA expression. The LCM results for c-Fos and Fra-2 were confirmed by riboprobe ISH. These results suggest that Fra-2 also participates in CTA learning. To identify other genes co-expressed in specific cells, we are using c-Fos-LacZ transgenic mice to identify Fos-positive cells for LCM analysis. Supported by NIDCD03198.

Regulation by L-leucine of system A amino acid transport in neurons and glial cells. D. L'HEUREUX-BOURON, A. BLAIS, J.F. HUNEAU, G. FROMENTIN, D. TOME. *Unit INRA/INAPG 914 Physiol Nutr and Feeding Behavior, Paris, France.*

The mechanisms by which the brain rapidly detects variations in essential amino acids availability remain unclear. Threonine deprivation has been shown to rapidly stimulate system A amino acid transporter SAT1 in neurons but not in glial cells from specific brain area. This study investigated the effect of L-leucine availability on system A amino acid transport activity in primary cultures of neurons and glial cells obtained from different brain regions, ie anterioir pyriform cortex (APC), ventro-median hypothalamus (VMH) area postrema (AP) and arcuate nucleus (ARC). The activity of system A amino acid transport was investigated using the non-metabolizable amino acid analogue *a*-(methylamino)-isobutyric acid (MeAIB). Increasing leucine availability produced a rapid increase in intracellular leucine concentration in the different cell type and a rapid transient increase in glutamate and glutamine glial cells. A one fold increase in leucine concentration did not modify system A activity in glial cells and VMH neurons whereas it was moderately increased after 6 h (from 10 to 40%) and significantly increase after 24 h in APC, AP and ARC neurons (75%, 100% and 75% after 24 h, respectively). This increase was not correlated to changes in SAT1 or SAT2 mRNA expression. This study confirms that neuron and glial cells from specific brain area respond to amino acids availability by specific pathways. In contrast to threonine deprivation, an increased leucine availability did not produce a rapid (i. e. less than an hour) response of system A from specific neuron population whereas it rapidly and transiently produced an increase in glial cell glutamate concentration.

Beneficial and side-effects of a long-term consumption of a high protein diet in rats. M. LACROIX, C. GAUDICHON, J.F. HUNEAU, V. MATHE, C. MORENS, D. TOME. *Unit INRA/INAPG 914 Nutr Physiol and Feeding Behavior, F75231 Paris cedex 05, France.*

The long term effects of a high protein diet on a broad range of parameters have not been investigated. We studied the beneficial and side effects of a high-protein diet in rats over a period of 6 months. 48 Wistar male rats received either a normal-protein (NP: 14% protein) or high-protein (HP: 50% protein) diet. Dietary and water intake, detailed body composition, plasma hormones and nutrients, liver and kidney histopathology, hepatic markers of oxidative stress and detoxification and the calcium balance were investigated. The energy intake of HP rats was 13% lower that of NP rats. In contrast, their water ingestion was 50% higher. After 6 months, HP rats showed a sharp reduction in white adipose tissue (48%) and lower basal concentrations of triglycerides, glucose, leptin and insulin. Total and LDL cholesterol where similar in both groups. Oral glucose tolerance tended to be improved in the HP group, but not significantly. No major alteration of liver and kidney where found in HP rats whereas NP rats exhibited massive hepatic steatosis. The calcium balance was unchanged and detoxification markers (GSH and GST) were moderately enhanced in the HP group. Our study suggests that the long-term consumption of a HP diet in male rats has no deleterious effects and could even prevent metabolic syndrome.

Molecular neuroanatomic characterization of central leptin targets. J.L. LACHEY[a], S.M. STERNSON[b], C.E. LEE[a], J.K. ELMQUIST[a], J.M. FRIEDMAN[b]. [a]*Departments of Medicine and Neurology; Division of Endocrinology, Beth Israel Deaconess Medical Center; Program in Neuroscience, Harvard Medical School, Boston, MA;* [b]*Howard Hughes Medical Institute, The Rockefeller University, New York, NY, USA.*

Leptin is a circulating adipocyte hormone that relays the condition of peripheral energy stores to the brain. Centrally, leptin signaling occurs via the long-form of its receptor (ObRb). Leptin-sensitive cell groups are concentrated in brain regions that regulate energy balance and neural-specific disruption of the ObRb leads to an obese phenotype indicating that leptin acts directly in the brain to regulate food intake and body weight. Despite the clear importance of ObRb in the CNS, the sites expressing the signaling form of the receptor have remained difficult to determine. To facilitate the identification of ObRb, we have constructed mice that express Cre-recombinase (Cre) specifically in neurons expressing ObRb mRNA. We crossed these mice with reporter mice designed to express yellow fluorescent protein (YFP), a variant of green fluorescent protein, only in the presence of Cre expression. The offspring resulting from this cross express YFP only in ObRb-producing cells and therefore, can be used to identify and accurately define the localization of ObRb in the mouse brain. Consistent with previous reports of ObRb mRNA distribution, high levels of YFP-IR are found in hypothalamic regions including the lateral hypothalamic area, dorsal medial nucleus and the arcuate nucleus. Extrahypothalamic areas containing YFP-IR cells include the dorsal raphe nucleus, the superior lateral parabrachial nucleus and the dorsal vagal complex. This mouse model provides a powerful tool for determining the chemical properties of ObRb-containing cells.

Lithium-induced gene expression in the rat hypothalamus. J.Y. LEE[a], J.H. LEE[b], D.G. KIM[a], J.W. JAHNG[a]. [a]*Deparment of Pharmacology, BK21 Project of Medical Science, Yonsei University College of Medicine, Seoul, 120-752, Korea;* [b]*Department of Oral and Maxillofacial Surgery, Seoul National University College of Dentistry, Seoul, 110-744, Korea.*

Intraperitoneal lithium chloride at high doses activates the hypothalamic-pituitary-adrenal (HPA) axis, induces conditioned taste aversion (CTA) learning. The hypothalamus is located in the center of HPA axis. We examined lithium-induced gene expression in the rat hypothalamic tissues at different time points, in order to determine underlying molecular mechanisms which lithium activates the HPA axis. Male Sprague–Dawley rats (280–330 g) were decapitated 1 or 6 h after an intraperitoneal injection of LiCl (0.15 M, 12 ml/kg) or physiologic saline, the hypothalamic tissues rapidly dissected on ice and homogenized with lysis buffer. The hypothalamic protein samples were separated on 2-D gels, and peptide sequence of the coomassie stained spots, which had increased density in the LiCl treated samples compared with the saline controls, were analyzed by MALDI-TOF peptide analysis system. One hour after LiCl, when lithium-induced c-Fos expression is heavily detected in the hypothalamus, gene expressions of a chaperon molecule, mitochondrial enzyme, sarcomeric protein and intermediate filament binding protein were detected to be increased up to 2 fold by LiCl. Six hour after LiCl, when most of the transient c-Fos expression disappears, expression of the genes which are involved in cellular differentiation and communication was increased by LiCl. These results suggest that LiCl at high doses may acutely induce the hypothalamic expression of various genes, and these genes may take a role in the functional plasticity, which occurs during CTA formation. Supported by KISTEP (JWJ).

Positive feedback circuit relating dietary fat, circulating triglycerides and hypothalamic peptides: possible role in producing large meals. S.F. LEIBOWITZ, G.-Q. CHANG. *The Rockefeller University, New York, N. Y. 10021.*

Certain peptides injected into the hypothalamus of rats, including galanin and the orexins, stimulate feeding and produce a stronger response on a high-fat diet than on a high-carbohydrate diet. Moreover, studies with chronic dietary manipulations demonstrate that consumption of a high-fat diet stimulates the expression of these feeding-stimulatory peptides. Recent evidence suggests that these 'fat-stimulated' peptides are potentiated by shorter periods of fat consumption, as short as 2 h. In different feeding paradigms, the expression levels of these peptides, galanin in the paraventricular nucleus and orexins in the perifornical lateral hypothalamus, are strongly, positively correlated with circulating lipids, particularly levels of triglycerides. A possible role of elevated lipids in producing this peptide change after a meal is further suggested by the findings that injections of lipids stimulate galanin and orexin expression within 2–4 h, and inhibitors of fat metabolism reduce peptide levels. This evidence demonstrates that dietary fat can alter hypothalamic peptides within a brief period, in response to changes in circulating metabolic fuels or their oxidation. Whereas a sustained increase in food intake is known to activate adipostatic responses that may limit lipid storage by reducing food intake, an increased availability of nutrients provided by a non-homeostatic, positive feedback circuit may have a physiological function under conditions when food is scarce and periods of gorging, perhaps involving mechanisms of reward, are essential to survival. This 'vicious cycle', between dietary and circulating fats and hypothalamic peptides, may contribute to the large meal size and overeating generally associated with fat-rich foods.

Reversal of hormone concentrations during phases of body weight loss with or without PEG-OB. M.P.G.M. LEJEUNE, C.J. MUKSHORN, W.H.M. SARIS, M.S. WESTERTERP-PLANTENGA. *Department of Human Biology, Maastricht University, P.O. Box 616, 6200 MD Maastricht, The Netherlands.*

The aim of the study was to investigate the effects of weight loss with or without pegylated recombinant leptin (PEG-OB) on the blood parameters ghrelin, adiponectin, IGF-1, insulin and glucose. We performed a randomized double blind placebo controlled trial in 24 overweight men (BMI: 28.8 ± 0.3 kg/m^2; 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. At day 1, 25, and 46 a blood sample was taken after an overnight fast, and body weight (BW) and satiety were measured. During phase 1 (day 1–25) the rate of BW loss was significantly higher in the PEG-OB compared to the placebo group (0.38 ± 0.07 vs 0.32 ± 0.06 kg/d, $P < 0.05$). The rate of BW loss during phase 2 (day 25–46) was 0.24 ± 0.08 and 0.18 ± 0.09 kg/d, respectively ($P = 0.07$). In both groups the rate of BW loss during phase 1 was significantly higher compared to phase 2 ($P < 0.0005$). During phase 1 the concentrations of insulin, glucose, adiponectin and IGF-1 decreased significantly in both groups. During phase 2 the concentrations of adiponectin, IGF-1 and ghrelin increased again. In the PEG-OB group the initial decrease and subsequent increase in ghrelin paralleled the increase and decrease in satiety. We conclude that BW loss induced decreased plasma levels of insulin, glucose, adiponectin, IGF-1 and ghrelin. However, when the rate of BW loss decreased these changes were reversed.

Injection of neuropeptide W into the paraventricular nucleus of the hypothalamus increases food intake. A.S. LEVINE, R. WINSKY-SOMMERER, S. HUITRON-RESENDIZ, M.K. GRACE, L. DE LECEA. *Minnesota Obesity Center, Minneapolis, MN 55417; The Scripps Research Institute, La Jolla, CA 92037.*

Neuropeptide W (NPW) is an endogenous ligand for the G protein-coupled receptor 7 (GPR7). There are two forms of the peptide designated as neuropeptide W-23 (NPW23) and neuropeptide W-30 (NPW30). In the current study we found that intracerebroventricular administration of NPW23 increased c-Fos immunoreactivity (IR) in a variety of brain sites, many of which are involved in the regulation of feeding. We also noted that cFos IR levels were increased in hypocretinergic neurons in the perifornical region of the lateral hypothalamus (LH). We then studied whether injection of NPW23 into the paraventricular nucleus of the hypothalamus (PVN) and the LH increased food intake during a 24 h time period. Intra-PVN injection of NPW23 at doses ranging from 0.1 to 3 nmol increased feeding for up to 4 h and doses ranging from 0.3 to 3 nmol increased feeding for up to 24 h. In contrast, only the 3 nmol dose of NPW23 increased feeding after administration into the LH. Together, these data suggest a modulatory role for NPW in the control of food intake. Supported by funds from the Department of Veterans Affairs and the National Institutes of Health.

Environmental influences on human eating behavior. D.A. LEVITSKY, I. SUNIL, F. SKURPSKI. *Division of Nutritional Sciences, Cornell University, Ithaca, NY 14853-6301.*

The degree to which our environment affects human energy intake determines the degree to which obesity is caused not by biology, but rather by our environment. Two studies were performed to examine this question. The first examined the role of the variety of food offered has on the amount of food consumed. In this study the number of foods offered in a buffet setting was varied and the amount of food selected and consumed was measured. The second study examined the how much food that is consumed by people with whom one is eating affects the amount of food selected and eaten. The results of these studies will have important implications for policies and programs aimed at reducing, or reversing, the high rate of obesity in our country.

Targeted lesion of NPY receptor-expressing neurons in the basomedial hypothalamus: changes in NPY, AGRP and CART gene expression and feeding behavior. A.-J. LI, K. BUGARITH, S. RITTER. *Department of VCAPP, Washington State University, Pullman, WA 99164-6520, USA.*

Hypothalamic gene expression of feeding-related neuropeptides and feeding behavior were investigated in rats after injection of a novel neuropeptide Y (NPY) receptor-targeted-toxin into the basomedial hypothalamus (BMH). This ribosomal toxin, saporin conjugated to NPY (NPY-SAP), has been designed to produce targeted lesions of cells expressing NPY receptors by receptor-dependent internalization of saporin into the cytosol. Binding studies revealed that NPY-SAP binds to brain NPY receptors with a higher affinity than NPY itself. Bilateral BMH injection of NPY-SAP (48 ng/100 nl) reduced NPY, agouti gene-related protein (AGRP) and cocaine and amphetamine-regulated transcript (CART) mRNA expression in the arcuate nucleus (Arc) to $< 10\%$ of control levels, as quantitatively assessed in situ hybridization studies. These results indicate that NPY/AGRP and CART/proopiomelanocortin (POMC) neurons, both known to express NPY receptors, were almost completely destroyed by NPY-SAP. Feeding studies showed that BMH injections of NPY-SAP (12–48 ng/100 nl) produced significant hyperphagia and a dose-dependant increase in body weight. Further analysis showed that the increase in food intake was due entirely to increased daytime feeding. Taken together, these results show for the first time the efficacy of NPY-SAP for lesioning neurons that express NPY receptors. Results also suggest a role for Arc NPY receptor-expressing neurons in the inhibition of feeding during the light phase of the circadian cycle.

Comparative 2D difference gel analysis of hypothalamus protein expression pattern of myostatin knockout mice with clenbuterol treatment. J. LIN, K.A. PAGE, M.A. DELLA-FERA, T.M. ANDACHT, D.L. HARTZELL, C.A. BAILE. *Departments of Animal and Dairy Science and Foods and Nutrition, and Proteomics Resource Facility, University of Georgia, Athens, GA 30602-2771, USA.*

Myostatin, a member of the TGF-β family of growth factors, inhibits muscle growth. Myostatin knockout (KO) mice have increased skeletal muscularity and decreased adiposity, but no difference in feed intake and body weight compared to wild type (WT) mice. We used two-dimensional difference gel electrophoresis (DIGE) analysis to compare global hypothalamic protein expression patterns in adult KO and WT mice treated with clenbuterol, a β2-adrenergic receptor agonist, or control. Mice ($N = 10$) were given either 0 or 200 ppm clenbuterol in food for 3 weeks. Proteins from dissected hypothalami were extracted in 5 M urea, 2 M thiourea, 4% CHAPS and 15 mM Tris buffer (pH 8.3) with sonication, followed by buffer exchange and concentration through filter centrifugation. 50 μg samples were labeled

with 3 different fluorescent CyDyes: Cy3 for WT, Cy5 for KO samples and a Cy2-labeled pooled sample for internal standard. A pair of the differently labeled samples, plus 50 μg pooled sample, were co-separated on the same 2D gel (pH 3–10, 8–15% gradient). In KO mice, 46 proteins had increased levels and 36 proteins had decreased levels compared to WT ($P < 0.05$). In clenbuterol treated mice, 14 proteins had decreased levels and 26 proteins had increased levels compared to control ($P < 0.05$). Our results indicate that hypothalamic protein expression pattern is affected by both myostatin gene knockout and clenbuterol treatment, and demonstrate that alterations in muscle and fat mass can affect hypothalamic protein expression patterns. DIGE analysis provides a powerful tool for comparative proteomics. Supported in part by Georgia Research Alliance Eminent Scholar endowment (CAB).

Central melanocortin signaling pathway is required for enterostatin effects. L. LIN, D.A. YORK. *Pennington Biomedical Research Center, 6400 Perkins Road, Baton Rouge, LA 70808, USA.*

Enterostatin selectively inhibits the intake of dietary fat after both central and peripheral administration. Brain microinjection studies have shown that a central site of action is the central nucleus of amygdala. Injection of enterostatin in this area induces c-Fos expression in hypothalamuic regions including arcuate nucleus. The objective of this study was to determine if the melanocortin system is involved in the response to enterostatin. Male Sprague–Dawley rats or melanocortin-4 receptor knock out (MC-4R KO) mice on C57/BL6 background and their wild type controls (WT) were adapted to a high fat diet (56% energy as fat). Unilateral chronic amygdala cannulas were implanted in rats. Enterostatin (0.1 nmol) or saline vehicle (0.1 ml) was injected into the amygdala; rats were sacrificed 2 h later by cardiac perfusion with paraformaldehyde. Brain sections were subjected to double label immunohistochemistry to visualize both c-Fos and α melanocyte-stimulating hormone (MSH). The number of c-Fos/α MSH double-labeled cells in the arcuate nucleus significantly increased after amygdala enterostatin injections in the rat. Icv administration of enterostatin reduced the intake of a high fat diet in wild-type mice (40% reduction) but had no effects in MC-4R KO mice. Peripheral injection of enterostatin suppressed the feeding in both WT and MC-4R mice (28% and 30% inhibition). The data demonstrate that arcuate melanocortin signaling is required for the response to amygdala enterostatin but suggest that MC-4 receptor activity is not required for the response to peripheral enterostatin. Supported by grant NIDDK 45278.

Fat and sucrose-energy substrates or reward signals? A. LINDQVIST, J. MEI, A. ANDREASSON, C. DORNONVILLE, D.E. LA COUR, C. ERLANSON-ALBERTSSON. *Department of Cell and Molecular Biology, Biomedical Center, C11, University of Lund, S-221 84 Lund, Sweden.*

Diets rich in fat and sucrose lead to overeating and obesity. We examined the importance of the reward system in relation to the energy homeostasis system during intake of palatable food containing fat and/or sucrose in rat. As candidate molecules for the reward system we investigated the opioid peptide expression in stomach and brain and their receptors and as candidate molecules for the energy homeostasis we chose ghrelin and leptin. Four different diets were tested, low-fat (control), low-fat + sucrose, high-fat and high-fat + sucrose. We found that all three diets caused hyperphagia compared to control, the most pronounced hyperphagia being the low-fat + sucrose diet. A short-term decrease of ghrelin expression in stomach was measured with the three palatable diets, whereas stomach leptin was unaffected. The expression of the opioid peptide β-endorphin in stomach was increased and both kappa- and mu-opioid receptors decreased in the stomach and in the brain. Uncoupling protein 2 expression was upregulated, both in stomach and in brain. We conclude that there is a short-term defence against the palatable food in rat by a reduction of hunger signals, whereas in the long-term the reward system takes over and promotes hyperphagia and overweight. Uncoupling protein 2 does not protect against obesity, but may be important to protect the organism against free oxygen radicals during high-fat intake. It thus seems that fat and sucrose are interpreted by the body rather as rewarding molecules than as energy substrates.

The conundrum of weight suppression: findings from three studies. M.R. LOWE, R. ANNUNZIATO, M. BUTRYN, E. DIDIE, C. OCHNER. *Drexel University, Philadelphia, PA.*

Weight suppression (WS) refers to the loss of a significant amount of weight (e.g. at least 10%) that is sustained for a lengthy period of time (e.g. at least 1 year). Past research has suggested benign consequences of WS (e.g. weight suppressors regulate their eating after a preload and show reduced sweetness preferences). However, we have conducted three recent studies that have produced more problematic associations with WS. In Study I, WS and several measures of restraint and overeating were used to prospectively predict weight gain during the freshman year of college. WS was the only predictive measure, with high suppressors gaining significantly more weight than low suppressors. In Study II, WS prospectively predicted amount of weight gain among bulimic patients during an inpatient stay; those highest in WS gained 4 times more weight than those low in WS. Finally, in a reanalysis of a previously published trial on cognitive-behavior therapy for bulimia, we found a strong relationship between pre-treatment WS and treatment outcome; drop-outs were twice as high in WS as nonabstinent completers, who in turn were twice as high in WS as abstinent completers. These findings indicate that metabolic and/or appetitive consequences of weight suppression make weight regain more likely.

Amylin's anorectic effect does not depend on an intact central nucleus of the amygdala (CeA). T.A. LUTZ, B. CETTUZZI. *Institute of Veterinary Physiology, Vetsuisse Faculty of the University of Zurich, 8057 Zurich, Switzerland.*

The anorectic hormone amylin specifically activates AP neurons and also leads to a strong expression of c-Fos protein in the nucleus of the solitary tract (NTS), lateral parabrachial nucleus (lPBN) and central nucleus of the amygdala (CeA). Lesions of the AP or the lPBN ablate peripheral amylin's satiating effect, and they also block the amylin-induced c-Fos expression in the CeA. We now tested whether the amylin-induced activation of CeA neurons is a necessary component in the signalling cascade of amylin's anorectic effect. We produced rats with an electrolytic lesion in the CeA (CeA-X) and compared the effect of amylin on food intake in these rats to sham-operated controls (SHAM). Post-mortem histology confirmed lesion of the CeA in the area where amylin-induced c-Fos is usually observed. Amylin (IP injection in 24 h food deprived rats; 5–10 μg/kg) similarly reduced food intake in SHAM and CeA-X rats (e.g. 1 h food intake, SHAM control 7.8 ± 0.5 g vs. amylin [10 μg/kg] 4.3 ± 0.2 g [$P < 0.001$]; CeA-X 6.8 ± 0.8 g vs. 3.5 ± 0.4 g [$P < 0.01$]). CCK (3 μg/kg) also produced a similar reduction of food intake in SHAM and CeA-X rats. We conclude that although anorectic doses of amylin induce c-Fos expression in the CeA, an electrolytic lesion of the CeA does not influence amylin's anorectic effect. The similar finding with CCK confirms previous reports. The activation of CeA neurons seen after peripheral amylin administration therefore seems to be unrelated to amylin's (or CCK's) satiating effect. The role of amylin-induced CeA activation remains to be clarified in future studies.

Eating as a distraction from stress: An experience-sampling study. M. MACHT, C. HAUPT, H. ELLGRING. *Institute for Psychology, University of Wuerzburg, 97070 Wuerzburg, Germany.*

The emotion regulation hypothesis of stress-induced eating was examined. Students ($n = 22$, 11 female, 11 male) awaiting an exam and control subjects ($n = 20$, 11 female, 9 male) were assessed 3 to 4 weeks and 3 to 4 days before the exam. They were given a pager, which beeped ten times a day at random intervals. Upon each signal, participants rated their emotional state and motivation to eat. If they had eaten since the last signal they reported characteristics of their actual eating behavior. Compared to control subjects, students awaiting an exam reported higher emotional stress and an increased tendency to eat in order to distract themselves from stress. Results indicate that emotion regulation eating is experienced in a non-clinical population during real-life stress and is mediated by distraction.

Emotion-induced changes of eating: toward a unifying framework. M. MACHT. *Institute for Psychology, University of Wuerzburg, 97070 Wuerzburg, Germany.*

A major problem for the study of emotion-induced changes of eating is their variability. On the one hand, individuals differ in eating responses to emotions. For example, 'stress eaters' increase, but 'stress fasters' decrease food intake in response to emotional stress. On the other hand, emotions differ in their effects on eating. For example, fear may decrease, but sadness may increase the motivation to eat. In other words, the effects of emotions on eating vary depending on individual characteristics and emotion features. Traditional approaches emphasized the study of individual characteristics, but ignored the role of emotion features. Thus, the variability of emotion-induced changes of eating has not been explained convincingly. The basic assumption of this presentation is that any change of eating induced by an emotion results from an interplay of four variables: emotions as input variables, eating responses as output variables, a number of physiological and psychological processes as mediators, and, individual characteristics as moderators. From this assumption, the fundamental questions for a scientific study of emotion-induced are derived: Which emotions change eating? Which eating responses are induced by emotions? Which processes mediate emotion-induced changes of eating? Which individual characteristics moderate effects of emotions on eating? I summarize the evidence on these questions and, based on this evidence, suggest five basic types of emotion-induced changes of eating: (1) emotional inhibition of eating, (2) emotion-congruent modulation of eating, (3) emotional disinhibition of restrained eating, (4) emotionally instrumental eating, and (5) emotional control of food choice. This typology can be used as a framework for future research.

The satiating potency of endogenous CCK increases after puberty in female rats. M. MANGIARACINA, A. WOLFE, A. AZZARA, G.J. SCHWARTZ, B.T. WALSH, N. GEARY. *Bourne Laboratory, NY Presbyterian Hospital–eill Cornell Medical College, White Plains, NY 10605.*

Because estradiol modulates the satiating potency of CCK in adult, cycling female rats (Asarian and Geary, Peptides 20 (1999) 445) and the effects of estradiol on eating appear only after puberty in rats (Wade and Zucker, J Comp Physiol Psychol 70 (1970) 213), we investigated the peripubertal development of CCK satiation. Fifteen female, 21-d old Long Evans rats were housed in computerized cages that monitored the time of removal of 45 mg chow pellets from a trough that was automatically replenished immediately following each pellet removal. Rats were monitored daily for vaginal canalization, which marks the first ovulation; after canalization, vaginal epithelial cytology was sampled daily. Thirty minutes before dark onset each day, rats were intraperitoneally injected either with 1 mg/kg devazepide, a selective antagonist of the CCK-1 receptor, or with the vehicle alone, according to an alternating schedule. Nocturnal spontaneous feeding was monitored. Devazepide had no significant effect on feeding before puberty, but stimulated feeding thereafter, with effects significantly larger two and 3 weeks postpuberty than one week after. Cycling was irregular during this period and no cyclic effects on eating were detected. The progressive stimulatory effect of devazepide on eating did not appear to be an artifact of increasing baseline food intakes due to the animals' growth, because devazepide's effect increased about 6-fold relative to baseline food intake (from about 2% of baseline before puberty to 12% 13–18 d afterwards). These data are a novel demonstration that the control of feeding by endogenous CCK increases around puberty in the female rat. Supported by MH 65024 (BTW), DK 47208 (GJS) and DK 54537 (NG).

Increasing protein content in a protein-fat, carbohydrate-free diet enhances fat loss during a mild but not a severe food restriction in the rat. A. MARSSET-BAGLIERI, G. FROMENTIN, D. TOMÉ, A. BENSAID, L. MAKKARIOS, P.C. EVEN. *Unit INRA/INAPG 914 Physiol Nutr and Feeding Behavior, Paris, France.*

This study evaluated the influence of the amount of protein in a protein-fat, carbohydrate-free diets fed ad libitum or during a mild (35%) or a severe (75%) food restriction: (1) Feeding rats ad libitum ($n = 6$ per group) with either a high-carbohydrate, low-fat diet (P21C69L10), a high carbohydrate, high-fat diet (P21C34L45), or a carbohydrate-free, high-fat, high-protein diet (P55L45), showed that the P21C34L45 diet significantly increased food intake and adiposity compared to the other diets. (2) Feeding rats ($n = 7$) either ad libitum or with diets varying in their protein and lipid content (P14C56L30, P30L70, P50L50 and P90L10) or pair-fed on the spontaneous intake of the P90L10 fed group that represented 85% of the energy intake of the P14C56L30 group (ie mild restriction), showed an inverse relationships between protein content and adiposity. (3) Feeding the same groups at 35% of the energy intake of the P14C56L30 group (ie severe restriction) showed non difference in body composition between groups. Taken together, these results showed that: (1) a high carbohydrate-high fat diet stimulates food intake and body adiposity, (2) a high fat content in the diet devoid of carbohydrate did not result in an increased food intake and body adiposity, (3) in ad libitum conditions or when food restriction is mild (25%) increasing protein content decrease food intake and body weight and may help in preserving lean body mass at the expense of fat mass, (4) in contrast, when food restriction is severe (75%) body weight and body composition are no more affected by the protein content.

Nociceptin/orphanin FQ and CRF-induced anorexia. M. MASSI, R. CICCOCIOPPO, D. ECONOMIDOU, A. FEDELI. *Department of Pharmacological Sciences and Experimental Medicine, University of Camerino, 62032 Camerino, Italy.*

Nociceptin/orphanin FQ (N/OFQ), the endogenous ligand of the NOP receptor, or the NOP receptor agonist Ro 64-6198 inhibit CRF-induced anorexia in rats. The present study evaluated the sensitivity of forebrain sites to the effect of N/OFQ on CRF-induced anorexia in male Wistar rats. Rats were implanted with bilateral cannulae for injections into the bed nucleus of the stria terminalis (BNST), the hypothalamic paraventricular nucleus (PVN), the ventromedial hypothalamus (VHM), the central amygdala (CeA), or with unilateral cannulae for injections into the dorsal raphe (DR) or the lateral cerebroventricle (LV). Animals were food deprived for 20 h, injected into the LV with 0.2 μg/rat of CRF or its vehicle, and given access to food 20 min later. N/OFQ, 0.05–1 μg/rat, was microinjected 10 min before CRF. In the BNST N/OFQ significantly reduced CRF-induced anorexia even at 0.05 μg/rat, while it was ineffective following injection in the PVN, VMH, CeA or DR at doses up to 1 μg/rat. In the LV a significant effect was detected at 1 μg/rat. Injected into the BNST N/OFQ, 0.05–1 μg/rat, modified neither food intake in food deprived rats (not injected with CRF), nor feeding in freely feeding rats. CRF evoked a statistically significant anorectic effect following injection into the BNST. The present findings show that the BSNT is highly sensitive to the antianorectic effect of N/OFQ. Since N/OFQ does not show affinity for CRF receptors, its effect on CRF-induced anorexia may be expression of functional antagonism. The present results, showing that the BNST is also sensitive to the anorectic effect of CRF, suggests that this area may be site for the functional antagonism of the two peptides.

Effect of increased food availability on food intake and body weights in rats. C.M. MATHES, N.E. ROWLAND. *Department of Psychology, University of Florida, Gainesville, FL 32611-2250, USA.*

Some writers have suggested that we live in an 'obesifying environment'. Not only does our food environment contain a variety of palatable foods, but the number of occasions that we encounter food in our everyday lives is high. These factors may play a role in food intake. Tordoff has shown recently that consumption by rats of various solutions increases as the number of drinking tubes increases. We now extend this line of investigation in two experiments. In the first, retired breeder female rats housed in standard polycarbonate cages received ad libitum food from jars in either one or four locations. The diet was either Purina Chow meal or a high fat diet (HFD) made of Chow plus vegetable shortening. Food intake and body weight gain differed as a function of the type of diet, but did not differ between one and four location groups. The rats subsequently were reassigned to groups in a study in which the temporal frequency of access to a palatable dessert was varied. A 60% sugar gel dessert was used, and rats additionally had ad libitum access to either Chow or HFD. Rats received dessert either for a single 8 h block (during their dark phase) or received the same gel for four 30 min periods every 2 h. Chow groups with continuous access to gel consumed more than those with intermittent access. HFD groups ate similar amounts of gel in both continuous and intermittent modes. Results were similar using a sweetened milk gel, which has a protein-to-calorie ratio similar to Chow. These results suggest that increased spatial or temporal feeding opportunities alone are not sufficient to overwhelm the normal homeostatic controls of feeding and satiety in these protocols.

A role for metabonomics in the MC4-R anti-obesity project. C.C. MATTHEWS, K.H. STRADER, A.F. RUSSELL, J.C. BIERMAN, K.L. MORAND, A.L. DEBEER. *P&G Pharmaceuticals.*

Agonism at the melanocortin 4 receptor (MC4-R) has been well-documented to produce anorectic effects. Metabonomics utilizes NMR for the evaluation of changes in metabolite levels of biofluids in response to a disease or experimentally controlled events, such as drug treatment and/or changes in diet. In the studies described below, we evaluated the feasibility of metabonomic analysis to (1) characterize the change in metabolite profile following drug exposure, and (2) rank order or eliminate candidate compounds based on desirable or undesirable metabonomic profiles. Serum and urine collected from lean and dietary-induced obese (DIO) rats treated with various MC4-R agonists were used for metabonomic analysis. The various treatments produced markedly different metabolic trajectories when graphed on a PCA plot. Two MC4-R agonists that produced both fat and lean loss separated sharply from the peptide agonist, MT-II, and vehicle treated rats. NMR analysis of serum revealed that the most pronounced metabolite changes were observed for β-hydroxybutyrate and creatine. Increased β-hydroxybutyrate levels in serum was evident in both lean and DIO rats treated with either MC4-R agonists or by food restriction as soon as 24 h after dosing, marking an increase of β-oxidation during the weight loss phase. A characteristic increase in both serum and urinary levels of creatine was detected in DIO animals treated compounds that also produce lean loss. A 7-day treatment with dexamethasone, a known cachectic agent, also resulted in a dramatic increase of creatine in serum, supporting creatine as a biomarker of protein degradation and/or muscle wasting. The results obtained thus far suggest the potential use of creatine, ketobodies and other metabolites as biomarkers for fat and lean loss in in vivo weight loss models.

Calcium deprivation increases the palatability of calcium-containing solutions in rats. S.A. MCCAUGHEY, C.A. FORESTELL, M.G. TORDOFF. *Monell Chemical Senses Center, Philadelphia, PA 19104.*

Rats deprived of dietary calcium show elevated intake of calcium-containing solutions relative to nutritionally replete controls. To assess whether this motivation to consume calcium involves changes in palatability, we measured taste reactivity of 8 replete and 9 calcium-deprived Sprague–Dawley rats. Each rat was implanted with an intraoral cannula to allow infusion of taste solutions directly into the mouth. A series of solutions were infused at 1 ml/min for 2 min, with each solution given once per day in an order that was counter-balanced across animals, and facial reactions were videotaped for analysis. Four ingestive behaviors, six aversive behaviors, and the number of passive drips were scored by scientists blind to the animal's group. Relative to replete controls, calcium-deprived rats had significantly higher total ingestive scores in response to all three calcium compounds tested (30 and 300 mM $CaCl_2$ and 30 mM calcium lactate). These results suggest that calcium appetite is accompanied by, and may in part be due to, an increase in palatability.

Antipsychotic induced weight gain: Psychosocial effects and potential psychosocial mediating variables. SUSAN L. MCELROY. *University of Cincinnati College of Medicine.*

Obesity and psychopathology are interconnected in complex and manifold ways. Obesity can both contribute to psychopathology and be contributed to by psychopathology. The pattern of association tends to vary radically by sex and form of psychopathology. Obesity can complicate the treatment of psychological disorders and vice versa. Dr McElroy will discuss evidence for these interconnections. She will then describe results from randomized clinical trils of weight loss compounds and programs among people being treated for psychological conditions.

Diabetic thirst: osmoreceptor stimulation by hyperglycemia in streptozotocin-induced diabetic rats. M.J. MCKINLEY, P.L. BURNS, B.J. OLDFIELD, K. SUNAGAWA, R.S. WEISINGER. *Howard Florey Institute, University of Melbourne, Victoria 3010, Australia.*

Strong thirst is a symptom of diabetes mellitus. It is thought that such diabetic thirst results from large fluid losses due to the glycosuria consequential to hyperglycemia. Studies in non-diabetic animals and humans have shown that systemically infused hypertonic glucose is ineffective at stimulating thirst. Thus, it is considered that diabetic thirst is a consequence of hypovolemia rather than of osmoreceptor stimulation. We have studied water drinking in rats made diabetic with streptozotocin. Daily water intake increased five-fold following streptozotocin treatment. Subcutaneous injection of an angiotensin II receptor AT1 antagonist caused only small reduction of water intake, indicating that angiotensin has only a minor role in this diabetic hyperdipsia. Expresssion of c-fos in the brains of diabetic rats was observed in the periphery of the subfornical organ, dorsal part of the organum vasculosum of the lamina terminalis, and in the median preoptic, supraoptic and hypothalamic paraventricular nuclei. The pattern of Fos-immunoreactivity in the lamina terminalis resembled that seen previously with hypertonicity rather than hypovolemia, indicating that osmoreceptors in the lamina terminalis may have been stimulated. Plasma and cerebrospinal fluid (CSF) [Na] and glucose levels showed that glucose did not equilibrate completely between plasma and CSF, and there were extremely high CSF Na levels, indicative of osmotic dehydration of the brain in diabetic rats. We also observed that while intravenous infusion of hypertonic 2 M glucose (1.8 ml/h) was ineffective as a dipsogen in normal rats, it was effective in diabetic rats. In addition, hyperglycemic diabetic rats drank water after bilateral nephrectomy. These data indicates that hypertonicity resulting from hyperglycemia may stimulate osmoreceptors for thirst in diabetic animals.

Perinatal MSG treatment attenuates fasting-induced bradycardia and metabolic suppression. M.M. MESSINA[#,a], S.A. EVANS[b], S.J. SWOAP[c], J.M. OVERTON[a,b]. [a]*Departments of Psychology Williams College, Williamstown, MA 01267;* [b]*Nutrition, Food and Exercise Science Williams College, Williamstown, MA 01267;* [c]*Program in Neuroscience, Florida State University, Tallahassee, FL 32306-4340; Department of Biology, Williams College, Williamstown, MA 01267.*

We studied the effect of arcuate nucleus (ARC) lesions induced pharmacologically by the perinatal treatment of monosodium L-glutamate (MSG) on the cardiovascular, metabolic, and behavioral responses to fasting. Saline and MSG-treated male Sprague–Dawley rats were instrumented with telemetry devices for measurement of mean arterial pressure (MAP) and heart rate (HR) and housed in room calorimeters at 23 °C for assessment of oxygen consumption (VO_2). At baseline, controls and MSG-treated rats had similar MAP (control = 95 ± 3; MSG = 91 ± 2 mmHg), HR (control = 323 ± 4; MSG = 323 ± 3 bpm), and VO_2 (control = 16.4 ± 0.6; MSG = 15.4 ± 0.4 ml/min). There were no differences in fasting-induced reductions in body weight or in food intake upon refeeding. In controls, 24 h of fasting substantially reduced HR (-33 ± 3 bpm) and VO_2 (− 1.2 ± 0.6 ml/min). In MSG-treated rats, the fasting-induced responses in HR (− 6 ± 5 bpm) and VO_2 (− 0.5 ± 0.6 ml/min) were clearly blunted. In subsequent experiments, we confirmed that MSG-treated rats exhibited intact capacity to both increase and decrease HR and VO_2 in response to cold (15 °C) and thermoneutral (30 °C) ambient temperatures. The results are consistent with the hypothesis that ARC signaling is requisite for intact homeostatic responses to reduced energy availability. Supported by NIH HL56732.

Dietary fat and environmental temperature interact to determine body fat content of leptin-treated mice. T.D. MITCHELL, R.B.S. HARRIS. *Department of Foods and Nutrition, University of Georgia, Athens, GA 30602.*

Peripherally administered leptin specifically reduces body fat in rodents by inhibiting energy intake and increasing energy expenditure but the relative contribution of each has not been elucidated. High-fat (HF) fed mice are leptin resistant but it is not known whether this is because they fail to reduce energy intake or to increase expenditure. We tested whether environmental temperature and the ability to increase heat loss influenced leptin responsiveness in low-fat (LF) or HF-fed mice. Ten-week old male C57BL/6J mice were fed LF (10% kcal fat) or HF (45% kcal fat) diet. After 5 weeks half of the mice were housed at 18 °C and half at 27 °C. Ten days later they were fitted with intraperitoneal miniosmotic pumps delivering PBS or 10 μg leptin/day for 13 days. Mice at 18 °C ate more than those at 27 °C. Diet and temperature influenced body fat so that HF-fed mice at 27 °C were the fattest and LF-fed mice at 18 °C were the leanest. Surprisingly, leptin increased carcass fat in HF-fed mice housed at 18 °C, despite a small inhibition of energy intake, but had no effect in any other group. In a second study LF- and HF-fed mice were housed at 18 °C or 23 °C and infused with leptin or PBS for 13 days. Leptin did not change food intake of any group but reduced body fat of LF-fed mice housed at 23 °C. These results suggest that loss of fat in leptin-treated LF-fed mice requires an increased energy expenditure, which is already elevated in the cold and is inhibited in a warm environment. HF-diet inhibits this mechanism and leptin may even reduce expenditure of HF-fed mice housed in the cold.

Dietary macronutrients and leptin signaling affect energy homeostasis. C. MORENS[#], V. SIROT, H. BARLA, A. SCHEURINK, G. VAN DIJK. *Neuroendocrinology, University of Groningen, PO Box 14, 9750 Aa Haren, The Netherlands.*

High-fat/carbohydrates (HF/C) diets are known to induce weight gain, whereas high-protein diets, particularly when they are high in fat (HF/HP) and low in carbohydrates like the popular 'Atkins diet', promote weight loss. While the underlying mechanisms are yet poorly understood, one hypothesis proposes that differential effects of macronutrient content on regulation of energy homeostasis require changes in the efficacy of leptin signaling in the CNS. To investigate this hypothesis, we studied the consequences of equicaloric diets of different macronutrient contents (i.e. C/P/F ratios of normal CHOW: 63/23/14, of HF/C-diet: 20/20/60, and of HF/HP-diet: 5/35/60) in control (Wistar) rats, in rats with a chronic impairment of a major leptin signaling pathway, the brain melanocortin (MC) system (caused by central infusion of SHU9119), and in Zucker fa/fa rats. HF/HP SHU9119-treated and control rats had lower food intake and body weight gain than corresponding HF/C rats, and were in fact indistinguishable from corresponding CHOW rats. Interestingly, compared to HF/C Zuckers, HF/HP Zuckers also had a reduced food intake (comparable to CHOW Zuckers), but this was not associated with lower body weight gain. Taken together those results show that leptin signaling, but not MC signaling, is required for weight reducing effects of HF/HP diets. Moreover, whatever the diet, SHU9119-treated and Zucker rats had elevated insulin and adiponectin levels. HF/HP SHU9119-treated and control rats had reduced glucose tolerance compared to HF/C and CHOW groups, whereas Zuckers were equally glucose tolerant. However, the CHOW-fed Zuckers presented a dysregulated insulin release and a reduced insulin sensitivity. Thus, we conclude that both diet composition and integrity of central leptin signaling pathways influence insulin sensitivity.

Hepatic 11β Hydroxysteroid Dehydrogenase -1 mRNA in obese and lean Zucker rats. A. MORIN, J. MOORE, E. ZAGER, D. CLEGG, L.M. BROWN, T.W. CASTONGUAY. *Department of Nutrition and Food Science, University of Maryland, College Park, MD 20742; Obesity Research Center, University of Cincinnati School of Medicine, Cincinnati, OH 45267.*

Glucocorticoids are essential factors in the expression of genetic and dietary obesities. However, until recently these hormones were thought to be merely permissive. Elevated circulating cortisol is not typically observed in human obesities. 11β hydroxysteroid dehydrogenase-1 (11β HSD-1) is an enzyme that can convert the inert glucocorticoid metabolite 11-dehydrocorticosterone back into the active hormone corticosterone. This reductase activity is thought to promote high levels of intracellular corticosterone in the tissues in which the enzyme is found. Last year we reported that rats made obese by feeding them a high fat diet had increased hepatic 11β HSD-1 mRNA when compared to controls fed a normal diet. In this study we set out to measure hepatic 11β HSD-1 in the livers of obese and lean Zucker rats fed a control diet. Total RNA was extracted from the livers of adult male obese and lean Zucker rats. cDNA was made from the RNA (Retroscript kit, Ambion, Inc., Austin TX), and RT-PCR was performed using primers flanking a 558 bp fragment of 11β HSD-1. Primers flanking 18S RNA were also used to control for variations in sample volume. All reactions used 800 ng of cDNA as template, and all were amplified for 30 cycles. PCR products were measured using a Model 2100 Bioanalyzer (Agilent Technologies Inc., Palo Alto, CA). Samples taken from lean rats had more than twice as much 11β HSD-1 message when compared to samples taken from obese rats. These data are consistent with previous reports of lower hepatic 11β HSD-1 message in obese Zucker rats. However these data are not consistent with our earlier report that obesity promotes increased hepatic 11β HSD-1 message. A discussion of some of the critical variables affecting the outcome of RT-PCR will be presented. (The authors want to thank B. Magnuson and M. Malik for their assistance with the RT-PCR.)

DOCA-induced sodium appetite decreases responding for lateral hypothalamic self-stimulation in the rat. M.J. MORRIS[#], E.S. NA, A.J. GRIPPO, B. HURST, A.K. JOHNSON. *Department of Psychology and the Cardiovascular Center, University of Iowa, Iowa City, IA.*

A sodium appetite arises when an animal is significantly depleted of sodium. While recent research has begun to focus on the rewarding properties of salty substances following depletion, there has been a relative lack of interest in the negative effects of chronic, unattenuated sodium appetite on the hedonic state of an animal. This study was undertaken to assess the effects of daily deoxycorticosterone acetate (DOCA) injections on sensitivity to rewarding electrical stimulation of the brain in the rat. Daily subcutaneous DOCA injections (10 mg/kg) produced a robust and persistent sodium appetite that developed within 48–72 h and continued for at least 2 weeks. DOCA-induced sodium appetite temporally corresponded with a decreased sensitivity to lateral hypothalamic self-stimulation (LHSS) reward. DOCA-treated rats that were denied access to sodium showed a rightward shift in LHSS current-response functions relative to their baselines, whereas controls did not. These findings suggest that a hormonal signal of a homeostatic imbalance can produce 'anhedonia', or a decreased responsiveness to rewarding stimuli, in the rat. It is suggested that persistent sodium appetite may be akin to a chronic stressor, and could decrease sensitivity to LHSS reward by directly affecting reward pathways within the brain.

Muscimol in the rostral lateral hypothalamus blocks orexin A-induced feeding. M.A. MULLET, C.M. KOTZ. *Veterans Affairs Medical Center and Minnesota Obesity Center, Minneapolis, Minnesota; and Departments of Medicine, and Food Science and Nutrition, University of Minnesota, St. Paul, Minnesota.*

Orexin A neurons in the posterio-lateral hypothalamic area (LHa) project widely throughout the central nervous system. Orexin receptors and orexin-containing fibers have been identified within the rostral LHa (rLHa), and orexin A injected into the rLHa dose-dependently stimulates feeding. Exposure of orexin A to cultured hypothalamic neurons influences GABA release, and LHa GABA injections inhibit feeding. We hypothesized that the GABA agonist, muscimol, would influence rLHa orexin A-induced feeding. To test this, we prepared male Sprague Dawley rats with unilateral cannulas directed at the rLHa. After recovery, ad libitum-fed animals were given the following rLHA treatments: vehicle + vehicle, vehicle + orexin A (500 pmol), muscimol (4, 12 or 20 ng) + orexin A (500 pmol), or muscimol (20 ng) + vehicle, at 1300 h. The first injection was given 15 min prior to the second. Treatments were given in a latin square repeated measures design, with random treatment assignment, and 72 h between treatments. Food intake was measured at 1 and 2 h. Data were analyzed by ANOVA followed by post-hoc t-tests to compare treatment means. There was a main effect of treatment on food intake in the 0–1 h interval but not in the 1–2 h interval. Post-hoc *t*-tests of the 0–1 h data indicate that all doses of muscimol (4, 12 and 20 ng) significantly and dose-dependently decreased rLHa orexin A induced feeding ($P = 0.0474$, $P = 0.0419$ and $P = 0.0015$ respectively). These results suggest that feeding elicited by rLHa administration of orexin A may be dependent upon decrements in local GABA.

The effect of Ghrelin on gastric vagal nerve afferents activity in rats. A. MURA, M. ARNOLD, W. LANGHANS. *Institute of Animal Sciences, Swiss Federal Institute of Technology (ETH) Zurich, 8603 Schwerzenbach, Switzerland.*

Recent studies suggest that the orexigenic peptide ghrelin stimulates feeding via vagal afferents. Ghrelin may decrease gastric vagal afferent activity, thus signaling hunger to the brain. To further test this hypothesis, we investigated the effect of ghrelin on vagal activity by recording vagal afferent discharge rate in anesthetized rats. Following anesthesia, a tube was inserted in the trachea, the stomach was ligated distal to the pylorus, and an intragastric tube was inserted in the esophagus to allow stomach distension. A catheter for drug delivery was inserted in the left carotid artery at the branch point of the celiac artery. The left cervical vagal trunk was exposed in the neck, a small bundle of nerve fibers was peeled off, and the distal cut end placed on tungsten metal wire electrodes. Only vagal afferents responding with an increase in firing rate to gastric load stimuli (1–3 ml of warm saline) were considered. Once a gastric load-sensitive fiber was identified ($n = 14$), ghrelin (300 pmol, 30 nmol, 3 μmol) was infused within 30 s and its effect on spontaneous firing rate, and on gastric load-induced increases in firing rate, was recorded for 30–60 min. Ghrelin reduced baseline activity and load-induced increases in firing rate only in 2 fibers at the highest dose (3 μmol). In all other fibers, all ghrelin doses did not reduce the firing rate under basal conditions or following gastric loads, whether ghrelin was administered before, during or after the loads. These results question the role of vagal afferent fibers in the feeding stimulatory effect of gherlin.

Nuclei involved in mediating the motivating and reinforcing properties of enhanced salt appetite. E.S. NA, T.G. BELTZ, R.F. JOHNSON, M.J. MORRIS, A.K. JOHNSON. *Department of Psychology and the Cardiovascular Center, University of Iowa, Iowa City, IA.*

Past studies have shown that rats that experience repeated Na^+ depletions show enhanced ingestion of 1.8% saline, under ad libitum conditions and in response to multiple deficits. The mechanisms underlying this increased Na^+ appetite have not been elucidated. The present experiment examined the role of the nucleus accumbens (NAc), basolateral amygdala (BLA), and subfornical organ (SFO) in Na^+ depletion-induced salt appetite. Rats were divided into 3 groups: furosemide (F) on 3 separate test days (3F); 2 vehicle (V) and a F (1F); 3 V (3V). On testing days, rats were given F or V and were given overnight access to water. Urine volume and Na^+ content were determined at 3 and 24 h. 24 h after injection, animals were given access to 1.8% NaCl and water and intakes were recorded for 60 min. After the Na^+ appetite test, rats were returned to home cages and given ad libitum access to 1.8% NaCl, water and food. Daily fluid intakes between depletions were recorded. On the final depletion, the Na^+ appetite test was omitted. Animals were sacrificed 27 h after the third test and Fos in the NAc, BLA, and SFO were quantified. 3F rats increased saline ingestion across depletions in daily intakes and in response to acute tests and also showed significantly more Fos than in animals in the 1F or 3V groups. These results demonstrate that animals with a history of multiple sodium depletions show an enhanced salt appetite and hence, may find the taste of saline more rewarding.

Effects of testosterone on body composition in a model of chronic psychosocial stress. M.M.N. NGUYEN[a,b], K.L.K. TAMASHIRO[a,b], L.Y. MA[b], D.A. D'ALESSIO[c], S.C. WOODS[b], R.R. SAKAI[b]. [a]*Neuroscience Program University of Cincinnati Medical Center, Cincinnati, OH 45267, USA;* [b]*Department of Psychiatry University of Cincinnati Medical Center, Cincinnati, OH 45267, USA;* [c]*Division of Endocrinology, University of Cincinnati Medical Center, Cincinnati, OH 45267, USA.*

Studies have consistently shown that chronic social stress results in body weight loss and reduction of plasma testosterone (T) levels. The Visible Burrow System (VBS) is a model used to study Long Evans rats that are housed in 4 male, 2 female colonies for 14 days. A dominance hierarchy forms among the males resulting in one dominant (DOM) and three subordinate (SUB) animals. Hierarchy associated changes in body weight, body composition, behavior and neuroendocrine stress measures have been observed. Of particular interest is the association between body weight, body composition, and T levels. SUB animals tend to have lower body weight and T levels compared to DOM. We propose that differences in body composition between DOM and SUB animals maybe due to the stress associated changes in circulating T levels. We have found that SUB animals lose a significant amount of adipose tissue and lean body mass compared to CON while DOM animals primarily lose adipose tissue when housed in the VBS. However, when VBS animals had T maintained at constant physiological levels, SUB animals did not lose as much body weight as the standard SUB. These data suggest that T may play a role in stress-induced body weight loss and changes in body composition. Supported by: NARSAD, Guggenheim Foundation, NSF, and NIDDK.

Biochemical sensors of nutrient abundance in the CNS. S. OBICI, A. POCAI, T. LAM, K. MORGAN, L. ROSSETTI. *Department of Medicine, Albert Einstein College of Medicine, Bronx, NY 10461, USA.*

All cells possess biochemical sensors of nutrient availability, which initiate adaptive responses to abundance or scarsity of fuel. In multicellular organisms, a complex system of neuronal and hormonal signals maintains energy balance and biochemical homeostasis. Nutrient sensing pathways are involved in the control of energy homeostasis by indirect mechanisms (increasing the expression and release of conterregulatory hormones, e.g. leptin, insulin etc.) or by directly modulating efferent signals in the Central Nervous System. Recent evidence has implicated malonyl-CoA and the metabolism of long-chain fatty acyl-CoAs (LCFA-CoAs) as cellular sensors of nutrient abundance in the hypothalamic arcuate nucleus. In particular, conditions which increase the levels of hypothalamic LCFA-CoAs decrease food intake and endogenous glucose production. In rat strains susceptible to diet-induced obesity, voluntary hyperphagia leads to an alteration of the hypothalamic lipid sensing pathway, suggesting that a disruption of these homeostatic responses may contribute to the pathophysiology of obesity.

Opposing effects of calcium and caloric intake on weight regain following a weight loss diet. C.N. OCHNER, M.R. LOWE. *Drexel University, Philadelphia, Pennsylvania.*

The purpose of these analyses was to determine the relationship between calcium and caloric intake (as predictors) and weight regain following a weight-loss diet. 103 women lost a nearly identical amount of weight ($M = 9.6$ kg) on a meal replacement-supplemented diet over a 6-month period. Caloric intake and calcium intake were both assessed using the Block Food Frequency Questionnaire (FFQ) and 5-day food records at 6 months (post-treatment) and at an 18-month follow up. All treatment ended at 6 months. Using change scores from 6 to 18 months, a regression analysis was used to examine the relationship between changes in calcium and caloric intake (predictor variables) and weight change (the outcome variable). When entered individually, neither change in calcium intake nor change in caloric intake was associated with change in weight using either measure. However, when entered simultaneously, increases in caloric intake predicted increased weight regain and increases in calcium intake predicted decreased weight regain using the FFQ. Results from food records revealed the same trend but failed to reach significance. Thus, each variable was predictive in the expected direction only when controlling for the other variable (a dual suppressor effect). Increases in caloric intake produce both greater weight gain and higher calcium intake. However, greater calcium intake may oppose weight gain, canceling out the effect of higher caloric intake. Therefore, when entered singly, neither variable predicts weight change. However, when holding the other variable constant, a positive relationship between caloric intake and weight gain, as well as a negative relationship between calcium intake and weight gain, is revealed.

Images of desire. M.L. PELCHAT, A. JOHNSON, R. CHAN, J. VALDEZ, J.D. RAGLAND. *Monell Chemical Senses Center, Philadelphia, Pennsylvania.*

Food craving (an intense desire to eat a specific food) is an extremely common psychological experience that has been linked to binge eating, snacking behavior, and maintenance of a varied diet. In addition, intense desire for foods (and sex) may be the primal source for cravings of all kinds (e.g. for illicit drugs, gambling, shopping). It is therefore surprising that so little is known about brain organization of food craving. We report here the first functional magnetic resonance imaging (fMRI) study to explicitly measure food craving (as opposed to hunger-induced desire). Twenty subjects participated in a study in which a two-part technique was used to produce the food cravings. First, the threshold was reduced through a diet manipulation (monotonous diet), without relying on hunger or other nutritional need. Second, cravings were triggered during the imaging sessions by having subjects imagine the sensory properties of favorite, but temporarily forbidden, foods (a cue-induction technique). Subjects were also asked to imagine the monotonous diet (which they did not crave). Signals generated while imagining the monotonous diet were subtracted from signals generated while imagining desired foods. This allowed us isolate craving-related signal changes while removing activation related to imagining food whether it is desired or not. Craving-related changes in blood oxygenation level dependent (BOLD) fMRI signal were identified in the hippocampus, caudate (dorsal striatum), and insula. The prominent representation of memory and sensory structures in the functional image is consistent with the sensory-specificity of food cravings (e.g. 'It has to be chocolate candy, a doughnut won't do'). These results also support the hypothesis that there are common brain mechanisms for food and drug cravings.

Leptin-induced satiation mediated by abdominal vagal afferents. J.H. PETERS, B.M. MCKAY, S.M. SIMASKO, R.C. RITTER. *Program in Neuroscience, College of Vet. Med., Washington State University, Pullman, WA 99164, USA.*

Most investigations of leptin effects on food intake have focused on brain sites of leptin action. However, vagal afferent neurons express leptin receptor mRNA. Furthermore, we have demonstrated direct activation of cultured vagal afferents by leptin. Most leptin-responsive neurons are also sensitive to CCK, which acts via vagal afferents to promote satiation. These observations, together with recent reports indicating that leptin is secreted by the stomach, suggest that leptin might play a direct role in the process of satiation via action on vagal afferents. In order to test whether leptin is capable of acutely decreasing short-term food intake we measured sucrose consumption following local leptin administration onto gastrointestinal targets. Leptin (1, 3, 10 μg) was applied via indwelling celiac arterial catheter and then sucrose intake was measured for 30 min. Celiac arterial infusion allowed us to apply small doses of leptin directly to the stomach and upper intestinal circulation, where vagal afferent innervation is the densest. We found that leptin dose dependently inhibited sucrose intake when infused through the celiac catheter but not when equal amounts were infused into the general circulation via a jugular catheter. This effect was abolished by bilateral subdiaphragmatic vagotomy. Circulating levels of leptin, sampled from the femoral artery, were similar between celiac and jugular infused animals. We conclude that leptin-induced activation of vagal afferents innervating the upper gastrointestinal tract reduces short-term food intake and may contribute to the process of satiation. This work was supported by grant number NS20561 and a grant from the Autzen Endowment.

Deprivation effects on meal size and macronutrient intake in humans. S. PLUNKETT[a], PHD, L. FONTENOT[a], J. DE CASTRO[b], PHD. *[a]Department of Psychology, Southeastern Louisiana University, Hammond, LA; [b]Department of Psychology, University of Texas at El Paso.*

Food intake is a regulatory process influenced by a host of variables. Under normal conditions, individuals compensate for changes in intake with appropriate compensatory increases or decreases. When environmental conditions, like food restriction, lead to a profound change in intake, individuals must consume more calories in order to make up for the restriction. Understanding the nature of this compensation is important to the investigation of the factors involved in intake regulation. Thus, the intakes of individuals who are trained fasters, as well as individuals who are not trained fasters were evaluated after 24 h of food restriction. How and when this compensation occurs was the focus of the present study. Individuals completed a 14 day diet diary and were randomly divided into two groups. One group recorded intake 1 week prior to and 1 week after the fast, and the other group recorded intake during two non-fasting weeks. The present findings indicate that compensation begins to occur partially immediately following the fast, but compensation also can be detected as late as 6 days after the fast. It appears that fasting participants made up the lost calories with larger meals, and with meals containing more fat, although meal pattern intake continued to follow its normal daily and weekly rhythm. Thus, 24 h of deprivation does not lead to aberrant eating patterns, but a compensation that occurs over time through increases in meal size and fat intake. This indicates that the magnitude of effect of compensated factors on intake in response to deprivation is weak and may be inhibited by uncompensated factors during weekdays.

The orexigenic effect of central ghrelin administration is enhanced in the absence of glucocorticoids. K. PROULX[a], T.P. VAHL[b], D.L. DRAZEN[a], S.C. WOODS[a], R.J. SEELEY[a]. *[a]Department of Psychiatry and Endocrinology; [b]Genome Research Institute, University of Cincinnati, Cincinnati, OH 45267-0559.*

Ghrelin is an orexigenic hormone made in the stomach and in the CNS. Little is known about the factors regulating ghrelin secretion. Since both ghrelin and corticosterone peak prior to meal onset, we hypothesized that ghrelin is stimulated by glucocorticoids. Plasma ghrelin levels were determined by RIA in fed and fasted adrenalectomized (ADX) and sham rats. Adrenalectomy significantly increased fasted plasma ghrelin compared to sham (4412.92 + 424.92 vs 2185.17 + 261.81 ng/dl). The orexigenic action of ghrelin is believed to be mediated through the NPY/AgRP pathway. Because ADX reduces the orexigenic actions of NPY and AgRP, we hypothesized that ADX would reduce ghrelin-induced hyperphagia. We measured food intake in ADX and sham at 30 min., 1, 2, 3 and 17 h following an i3vt injection of either ghrelin (1, 5, 10 μg) or saline. We found that ghrelin-induced food intake was significantly elevated in ADX compared to sham (5 μg: 633.83 + 135.46% vs 311.7 + 38.33% of saline intake at 2 h) and this effect was reversed by glucocorticoid replacement (355.52 + 21.99% vs 335.93 + 22.53% of saline intake at 2 h). In contrast, ip ghrelin administration (20, 40 and 80 μg/kg body weight) did not significantly increase food intake in either sham or ADX. So while these data do not support our original hypotheses, they do imply the existence of a regulatory feedback loop between glucocorticoids and ghrelin. Moreover, the enhanced ability of central ghrelin administration to stimulate food intake in the absence of glucocorticoids suggests the recruitment of orexigenic pathways independent of NPY/AgRP.

Withdrawal from extensive intake of chocolate cake mix batter by female rats induces more weight loss than observed after withdrawal from white cake mix batter. L.D. REID, K.J. BOSWELL, A.M. LACROIX, C.A. CAFFALETTE, M.L. REID. *Laboratory for Psychopharmacology. RPI, Troy, NY; Siena College, Loudonville, NY.*

Female rats were given the opportunity to take a batter made from chocolate cake mix for 24 h a day for 8 days along with their usual food and water. Another comparable group was given the opportunity to take batter made from white cake mix. Intakes of both batters were very similar (e.g. on last day of intake, mean intake of 20 and 19 g for chocolate and white, respectively). Upon termination of batter intake and across the following 24 h, the females previously taking chocolate batter lost a mean of 6.1 g (about 3% of their previous 3-day weight), whereas those taking white batter gained 0.8 g, $P < 0.005$. The major difference between the two mixes is the presence of cocoa powder in the chocolate mix. Withdrawal from extensive intake of ingesta containing cocoa powder induces a disturbance manifest in considerable weight-loss that is more extensive than that induced by withdrawal of equally palatable ingesta without cocoa. The extensive loss that can be interpreted as a sign of physical dependence similar to that seen with generally recognized addictive agents.

Behavioral and central neural activation effects of amylin agonist in neonatal rats. L. RINAMAN. *Univ. of Pittsburgh, Department of Neuroscience, Pittsburgh, PA 15260, USA.*

The pancreatic hormone amylin reduces food intake in adult rats via receptor-mediated activation of the area postrema (AP) and subsequent recruitment of hindbrain, hypothalamic, and limbic circuits. Amylin also stimulates drinking via actions at receptors in the subfornical organ (SFO) and recruitment of its hypothalamic targets. The present study investigated ingestive responses and neural activation in neonatal rats after i.p. injection of amylin receptor agonist (salmon calcitonin; sCT). Rat pups (2, 7, or 11 days old) were removed from their dam and held for 5 h in an incubator. Pups were weighed and injected with sCT (1 or 10 μg/kg) or vehicle (0.13 M NaCl) and returned to the incubator. 10 min later, one cohort from each age group was given access to warm milk on the floor, with amount consumed in 20 min defined as delta BW. A second cohort from each age group was perfused with fixative 70–90 min after i.p. injection. Brain sections were processed for cFos localization; some sections were double labeled to reveal noradrenergic and peptidergic neurons. Systemic sCT increased milk intake in a dose-related manner in 2-day old pups. Conversely, sCT had inconsistent and non-significant effects on milk intake in 7-day olds, and inhibited milk intake in 11-day olds. Systemic sCT robustly activated AP, SFO, and magnocellular hypothalamic neurons at each age, with age-related increases in cFos observed in the central amygdala, parvocellular paraventricular and lateral hypothalamus, and other central regions. These results suggest that sCT recruits dehydration-responsive neural circuits very early in development, whereas the anorexic effect of sCT is mediated by separate neural circuits that only become functional during the 2nd week postnatal.

The reinforcing efficacy of cocaine is increased following specific patterns of binge cocaine self-administration and abstinence. D.C.S. ROBERTS. *Department of Physiology and Pharmacology, Wake Forest University School of Medicine, Winston-Salem, NC 27101.*

The process of cocaine addiction in humans involves a transition from recreational drug use to compulsive drug-taking. To understand or study this behavioral phenomenon from a neurobiological perspective, behavioral models that reflect this process are necessary. In self-administration experiments with rats which use short daily sessions (2–3 h/day); stable patterns of drug intake are observed; thus limited access conditions fail to capture the transitional phases of the addiction process. A number of labs are now exploring other access conditions in an attempt to document progressive changes in drug taking behavior over time. In our lab, a progressive ratio (PR) schedule has been used to assess changes in the motivation to self-administer cocaine following various drug exposure conditions. While many high access conditions produce tolerance or have no effect on cocaine-reinforced responding, we have identified critical conditions that produce a robust increase in responding on a PR schedule. Round-the-clock access to cocaine (4 trails/h, 1.5 mg/kg/inj.) for at least a week coupled with a drug deprivation period results in an upward shift in the dose response curve. Thus it appears that binge-type drug intake and abstinence affect the reinforcing efficacy of cocaine. This model in conjunction with recently developed tools to characterize neurochemical and epigenetic changes will allow for the study of neural correlates of cocaine self-administration at time points that correspond to changes in reinforcing efficacy.

Brain processes that underlie the palatability of food. EDMUND T. ROLLS. *Department of Experimental Psychology, University of Oxford, Oxford OX1 3UD.*

During a meal, the pleasantness of the taste, smell, sight and texture of the food being eaten decreases to zero, while other can foods remain pleasant. This is sensory-specific satiety. As a result, more food is eaten if variety is provided, and sensory-specific satiety is a major determinant of the amount of food eaten in a meal (see Rolls, 1999). Sensory-specific satiety is not represented in the primate primary taste cortex or inferior temporal visual cortex, where neurons are not affected by feeding to satiety. These areas represent the identity of the stimulus. In the primate orbitofrontal cortex, neurons show sensory-specific satiety-related effects, decreasing their responses to the sight, taste, odour and texture (e.g. fat texture) of food to zero during feeding to satiety. Some sensory-specific satiety can be produced simply by tasting, smelling etc the food for 10 min without swallowing. These findings indicate that sensory-specific satiety is implemented by habituation with a time course of approximately 10 min of synaptic afferents onto orbitofrontal cortex neurons which represent the reward value or pleasantness of food, combined with a feedback effect of gastric distension. Recent neuroimaging studies show that sensory-specific satiety is reflected in activations found in the human orbitofrontal cortex.

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Fatty acid synthase and energy regulation. G.V. RONNETT. *Department of Neruoscience, The Johns Hopkins University School of Medicine, Baltimore, MD 21205.*

Fatty acid synthase (FAS) is a lipogenic enzyme that catalyzes the condensation of acetyl-CoA and malonyl-CoA to generate long-chain fatty acids. We and others have demonstrated that inhibition of FAS using the synthetic FAS inhibitor C75, administered centrally or peripherally, was able to reduce food intake and induce a profound loss of body weight. FAS is expressed in a number of brain regions, including arcuate and paraventricular nuclei (PVN) within regions that comprise the arcuate-PVN pathway. FAS co-localizes with neuropeptide Y (NPY) in neurons in the arcuate nucleus, suggesting that C75 may alter food intake via interactions within the arcuate-PVN pathway mediated by NPY. Indeed, C75 inhibits fasting-induced increases in NPY, supporting this hypothesis. We also observed that C75 treatment resulted in greater weight loss than in pair-fed controls. To investigate this paradox, whole animal calorimetry and in vitro studies of fatty acid oxidation (FAO) was performed and revealed that C75 also acts peripherally to increase FAO by activating carnitine palmitoyl-transferase-1 (CPT-1), the rate-limiting enzyme of FAO. We have recently investigated the cellular mechanisms of C75's action to shoe in vitro and in vivo that at least part of the anorexic effect of C75 may be due to modulation of AMP-activated protein kinase (AMPK), a known peripheral energy-sensing kinase. Collectively. these data suggest a role for fatty acid metabolism in the perception and regulation of energy balance.

Compensation for an increase in body fat caused by donor transplants into mice. C.R. ROOKS[a], T. BENNET[a], T.J. BARTNESS[b], R.B.S. HARRIS[a]. [a]*Department of Foods and Nutrition, University of Georgia, Dawson Hall, Athens, GA 30602;* [b]*Department of Biology, Georgia State University, Atlanta, GA 30303.*

Evidence for the regulation of body fat in experimental animals comes from lipectomized animals in which removal of one fat depot results in an increase in size of remaining depots. Less is known about the response of endogenous fat depots to an increase in body fat caused by fat transplanted from donor animals. In this study we tested whether mice changed the size of their endogenous fat stores if fat was added as subcutaneous transplants. In the first experiment each epididymal fat pad from donor mice was cut in half and placed ventrally in recipient mice, increasing body fat by approximately 10%. After 2 weeks there was no effect of the transplants on the size of endogenous fat depots or the size of adipocytes in epididymal fat depots. There was a substantial decrease in mass and adipocyte size in transplanted fat. Five weeks after surgery endogenous epididymal and retroperitoneal fat depots of recipient mice decreased, serum leptin was reduced and adipocytes in endogenous epididymal fat were significantly reduced in size, although cell number had not changed. The size of transplanted cells was the same as at 2 weeks. In a second experiment epididymal fat was placed as either dorsal or ventral subcutaneous fat transplants. Five weeks after surgery endogenous fat depots were decreased in all recipient mice but none of the differences reached statistical significance. These results suggest that mice have mechanisms to maintain total body fat mass that respond to an increase in the number of fat cells present.

Glucosensing neurons as CNS nutrient sensors. V.H. ROUTH. *New Jersey Med School, Newark NJ.*

Neurons within the hypothalamus change their firing rate in response to changes in extracellular glucose levels. These neurons exist in nuclei such as the arcuate (ARC) and ventromedial hypothalamic nucleus (VMN) which are important for the regulation of food intake and energy balance and/or body fat content. We have shown that the glucose sensitivity of glucosensing neurons is highly tuned to sense extracellular glucose levels within the physiological range. Moreover, glucosensing involves a complex convergence of pre- and post-synaptic mechanisms. That is, there are populations of glucosensing neurons which intrinsically sense glucose using mechanisms similar to that of the pancreatic β-cell. These neurons, as well as non-intrinsically glucosensing neurons, receive presynaptic input from other glucosensing neurons. In addition to sensing glucose, the activity of glucosensing neurons is also regulated by lactate. Surprisingly, the effects of lactate on glucosensing neurons are distinct and, in some cases, opposite to those of glucose. Glucosensing neurons are integrators of critical signals of energy balance, including insulin, leptin, neuropeptide Y and α-melanocyte stimulating hormone. Finally, glucosensing neurons are dysfunctional in rats which are prone to develop dietary obesity and type 2 diabetes mellitus. These data suggest that glucosensing neurons may play a role in CNS nutrient sensing. The mechanisms by which glucosensing neurons sense and respond to changes in extracellular nutrients will be discussed in this presentation.

Alcohol presentation in Polycose or beer vehicles and caloric compensation in rats. N.E. ROWLAND, N. NASRALLAH, K.L. ROBERTSON. *Department of Psychology, University of Florida, Gainesville, FL 32611-2250, USA.*

The disposition of alcohol calories is not well understood. Progress has been hampered in part by the low elective intakes of alcohol in many protocols using rodents, with the exception of inbred alcohol preferring strains. Typical alcoholic beverages consumed by humans invariably contain some additional calories in the vehicle. We have used this association in attempts to stimulate high elective alcohol intakes and then to examine compensation in intake of food in rats. Adult male and female Sprague–Dawley rats were given ad libitum access to Purina Chow and water, and were additionally presented with 5% or 10% alcohol in water or beer. Intakes of each commodity were recorded daily. Mean intakes of alcohol in beer (16.5 and 11.5 ml for 5 and 10% alcohol) were higher than in water (4.0 and 2.9 ml, respectively). Caloric adjustment was examined in rats with access to chow and 0, 5 or 10% alcoholic beer {the nonalcoholic beer base has ~0.21 kcal/ml}. Male and female rats consumed large amounts of nonalcoholic beer (>100 ml and >20 kcal/day) and males showed an exaggerated reduction in chow intake, such that total caloric intake fell by ~10%. Females showed quantitative caloric compensation. We performed similar studies using 5–10% alcohol in Polycose either as a solution or as a solid gel. Daily intakes were comparable to or higher than those observed with beer, and were higher with gel than solution. In both males and females, intake of chow was suppressed by more than the prediction from caloric content of the alcoholic gel.

Biological clock control of daily glucose homeostasis. M. RUITER, A. KALSBEEK, R.M. BUIJS. *Hypothalamic Integration Mechanisms, Netherlands Institute for Brain Research, 1105 AZ, Amsterdam, The Netherlands.*

The hypothalamic biological clock, located in the suprachiasmatic nucleus (SCN), receives light information via the optic nerve and sends the time-of-the-day message to the rest of the body. This happens via different (hormonal and neuronal) pathways. Thus, the body is able to anticipate the daily changes in activity, e.g. by adapting the energy availability for different organs to their specific needs. Previously, a daily rhythm in glucose tolerance, modulated by the SCN, has been shown in rats. Glucose uptake is highest at the onset of the activity period. It is not known, however, in which tissues most glucose is taken up and how the SCN modulates this uptake. Glucose uptake is regulated in several ways, insulin being the most well known stimulator. However, also insulin-independent glucose uptake occurs, e.g. in the brain, where glucose is necessary continuously. To investigate whether the SCN modulates insulin-independent and/or insulin-dependent glucose uptake, a small bolus of tritiated 2-deoxyglucose (^{3}H-2DG) was injected intravenously, with or without insulin, at different moments of the light-dark cycle. Afterwards, ^{3}H-2DG content of several tissues such as skeletal muscle, brain and adipose tissue was determined. Preliminary results indicate that non-insulin mediated ^{3}H-2DG uptake is not modulated by the SCN. Furthermore, we investigated the daily rhythm in plasma FFA concentrations, since it has been proposed that increased FFA concentrations modulate glucose uptake by inducing insulin resistance (the Randle-concept). Ongoing studies investigate which projection(s) to other hypothalamic areas the SCN may use to regulate peripheral glucose uptake. Target areas of the SCN are stimulated or inactivated by the administration of NMDA or TTX, respectively, through reverse microdialysis and ^{3}H-2DG uptake in peripheral tissue is determined. This work was supported by the Dutch Diabetes Foundation.

Adaptation to high-fat diet leads to short-term hyperphagia. D.M. SAVASTANO, M. COVASA. *Department of Nutritional Sciences, College of Health and Human Development, The Pennsylvania State University, University Park, PA 16802.*

Overconsumption of high-fat, hypercaloric diets are frequently associated with the development of obesity. We hypothesized that maintenance of rats on a high-fat diet would result in reduced sensitivity to satiation signals, thus leading to overconsumption of a high calorie food. To test this, we measured daily, three-hour intake of a hypercaloric, high-fat (HHF, 5.3 kcal/g) test food in rats maintained on either low (LF) or high (HF) fat, isocaloric (3.9 kcal/g) diets. During testing, one-half of each group received the HHF test food (LF/HHF; HF/HHF), while the other half received their respective maintenance diet (LF/LF; HF/HF). We found that rats maintained on a HF diet ate significantly more of the HHF food during the three-hour testing period compared to LF maintained rats (HF/HHF = 7.7 g vs. LF/HHF = 5.5 g; $P = 0.003$). Rats tested on their own maintenance diets had similar intakes (HF/HF = 3.2 g vs. LF/LF = 3.7 g), which were significantly lower ($P \leq 0.008$) than intakes of rats tested on a hypercaloric, high-fat diet. In a subsequent short-term choice preference test, rats exhibited an equal relative preference for HHF irrespective of their maintenance diets. There were no significant differences in total 24 h caloric intake between groups. However, 15-day total caloric intake was significantly higher ($P < 0.05$) in rats receiving HHF regardless of their maintenance diet. Overall, there was no significant body weight difference between HHF-tested rats. Additionally, while there was no significant difference in body weight gain between HF/HHF and HF/HF rats, LF/HHF rats gained significantly more ($P = 0.025$) weight compared to their respective control (LF/LF) rats. These results demonstrate that chronic ingestion of a high-fat diet leads to short-term overconsumption of a hypercaloric food compared to low-fat maintained cohorts.

Melatonin treatment influences hoarding behavior in rats. G. SCALERA. *Dip. Scienze Biomediche, Sez. Fisiologia, Universita' di Modena and Reggio Emilia, Via Campi 287, 41100 Modena, Italy.*

Leptin treatment, a protein encoded by ob gene and produced by white adipose cells, decreases food hoarding in Syrian hamsters. Melatonin (MLT) administration significantly decreases plasma leptin levels in rats. During light, plasma leptin is high and MLT is low; during dark, their concentrations are reversed. This reciprocal relationship may be due to MLT's inhibitory effects on leptin production, so that when plasma MLT is high leptin is comparably low and vice-versa. Three experiments were performed to verify the hypothesis that MLT administration may influence hoarding behavior in rats. Sixteen male Sprague–Dawley rats housed individually were kept on a 12:12 h L/D cycle, except as specifically noted; food and water were ad libitum, except during hoarding phase. Exp. 1 served to determine the hoarding baseline. Rats hoarding more than 70% of pellets scattered in the hoarding apparatus were designed as high hoarding (HH-rats), whereas rats hoarding less than 30% of pellets were designed as low hoarding (LH-rats). In Exp. 2, rats were injected s.c. by MLT (1 mg/kg b.w.) or by vehicle for 15 days in the morning and shortly after tested for hoarding behavior. Results show that MLT treatment increases significantly the number of pellets hoarded by LH-rats, but not by HH-rats. In Exp. 3, rats were exposed to 24 h continous light and tested for hoarding behavior lasting 3 weeks. At 2nd and 3rd week, HH-rats but not LH-rats significantly reduced the number of pellets hoarded. In conclusion, hoarding behavior is influenced by MLT treatment and by continous lightining which are inversely related to the plasma leptin concentration. These data may represent a functional and behavioral expression of the inverse relationship existing between plasma MLT and leptin.

Effect of exogenous CCK on 9–12 days old rat pups: independent ingestion and c-fos like immunoreactivity in brainstem, hypothalamic nuclei and central nucleus of the amygdala. M. SCHROEDER[#], O. MALKESMAN, D. HABA, A.-M. TORREGROSSA, G.P. SMITH, A. WELLER, S. BLUMBERG. *Department of Psychology, Gonda Brain Res Ctr, Bar-Ilan Univ., Israel; Bourne Lab, Department of Psychiatry, NY-Presbyterian Hosp-Cornell Univ Med Coll, USA.*

Previous research suggested that while exogenous CCK activates brainstem of newborn and adult rats, forebrain nuclei do not respond in newborn rats. To assess the emergence of CCK-responsive feeding- related nuclei, 9–12 days-old Sprague–Dawley rats received saline or 1.5, or 10 μg/kg CCK-8 intraperitoneally. In a 30-min independent ingestion test, saline and 1 μg/kg CCK had similar effects on % weight gain, but 5 or 10 μg/kg CCK significantly reduced subsequent intake. In a different group of pups, c-fos expression in NTS regions and hypothalamic subnuclei was examined. Five or 10 μg/kg CCK induced significant increases in neural activity in caudal, medial, commissural and intermediate NTS and paraventricular-, supraoptic-, arcuate-nuclei of the hypothalamus and central nucleus of the amygdala, compared to saline or 1 μg/kg CCK. No significant difference occurred between saline or 1 μg/kg CCK treatment in these subcortical nuclei. This suggests the emergence of postnatal maturation of neural connections between hind and forebrain by the age of 9–12 days in the rat. These results also raise the question whether CCKA receptors that mediate the action of CCK at low doses, located on the gastric and duodenal vagal afferent fibers, have matured at the age of 9–12 days in the rat.

Support: US-Israel Binational Science Foundation and Rich Center, Bar-Ilan University.

Effects of hunger level, fasting, and body composition measurements on pain threshold and tolerance. A. SCHULER, B. RAUDENBUSH, R. GRAYHEM. *Department of Psychology, Wheeling Jesuit University, Wheeling, WV.*

Previous research indicates that past experience with pain mediates future pain threshold and tolerance. In addition, level of body fat and susceptibility to external eating cues are highly correlated (as proposed by the Externality Hypothesis of Obesity). The present study was designed to combine such factors, and assess whether hunger pains play a mediating role in regards to pain threshold and tolerance. Utilizing a within-subjects design, participants completed the experimental protocol both after completing a 24-h fast and after consuming a meal until they were satiated. The order of the conditions was randomized. The protocol consisted of a cold pressor test, with submersion of the dominant hand and forearm into a 3 °C water bath. Ratings of pain were made on an 11-point scale every 30 s up to a maximum of 5 min. In addition, several participant variables (i.e., height, weight, gender, body composition) and personality tests (i.e., Profile of Mood States, NASA Task Load Index, Food Neophobia Scale) were recorded. Significant effects were found among the fasting and non-fasting conditions. While fasting, participants indicated greater pain tolerance (as measured by the total amount of time the participants were able to tolerate the cold pressor test), as well as decreased pain ratings over time. In addition, there was a significant interaction of body composition and condition, such that participants with larger body compositions were able to withstand the pain for a greater period of time under the fasting condition. These results provide additional support for the influence of both past pain experience and body fat level on mediating pain threshold and response.

Effects of beverage flavor on athletic performance, mood, and workload. A. SCHULER, A. RAWSON, B. RAUDENBUSH. *Department of Psychology, Wheeling Jesuit University, Wheeling, WV.*

Previous research indicates that the administration of peppermint odor can augment athletic performance and mood, and decrease workload demands. The present study extended those findings by evaluating athletic performance and physiological changes during the administration of flavored beverages. Utilizing a within-subjects design, athletes performed a 15-min modified treadmill stress test. At 3-min intervals, 50 ml of beverage (peppermint water, unadulterated water, or Gaterade sports drink) were consumed. In the control condition, no beverage was consumed. Pre- and post-testing physiological measurements were taken (blood pressure, pulse, oxygen concentration). In addition, ratings of mood (via the Profile of Mood States) and workload (via the NASA Task Load Index) were completed. No physiological changes were noted, however, both the peppermint and Gatorade sports drink conditions lead to greater ratings of personal performance and increased mood. These results provide additional support for the implementation of non-pharmacological methods to increase an athlete's performance and mood during exercise and/or competition. This study was funded by a grant from NASA to B. Raudenbush.

Sucrose motivation in sweet 'nontaster' (129P3/J) and 'taster' (C57BL/6J) mice. A. SCLAFANI. *Psychology Department, Brooklyn College of CUNY, Brooklyn, NY, USA.*

Sweet 'nontaster'129P3/J (129) mice consume less sucrose at low to intermediate concentrations (0.5–8%) than do 'taster C57BL/6J (B6) mice. The strains do not differ in intakes of concentrated (16–32%) sucrose solutions. Postingestive satiety limits intake of concentrated solutions, which may mask differences in sucrose avidity in the two strains. This hypothesis was investigated in male mice given sucrose vs. water operant licking tests. Sucrose (16% or 4%) was available 22 h/day through sipper tubes attached to bottles (BT) or to pumps activated by licking responses on fixed ratio (FR) or progressive ratio (PR) schedules. The FR schedule delivered sucrose (~0.025 ml) for every 20 licks emitted. PR schedules increased the lick requirement by 1 (starting at 20 licks) after every 8, 4, 2, or 1 reinforcements (PR8 + 1 to PR1 + 1). The 129 and B6 mice consumed similar amounts of 16% sucrose in BT and FR tests (~17 ml/day). In PR tests, as the schedule became more demanding, sucrose intake decreased in both strains to about ~7 ml/day. Yet, total licks increased with PR demand more in 129 mice than B6 mice as did lick 'break points' (to 358 vs. 302 licks/reward). B6 mice consumed more 4% sucrose than 129 mice in BT and FR tests (27 vs. 9 ml/day), but the strains did not differ in sucrose intake, licks, or breakpoints in the PR1 + 1 test. Thus, contrary to expectation, 129 mice were as or more motivated to obtain sucrose on lean reinforcement schedules compared to B6 mice. The sensitivity of sweet taste receptors is not the sole determinant of sucrose reward. Supported by NIH Grants DK-31135 and DK-59630.

Enhanced sweetener preference in sweet 'nontaster' (129P3/J) and 'taster' (C57BL/6J) mice after experience with sucrose. A. SCLAFANI. *Psychology Department, Brooklyn College of CUNY, Brooklyn, NY, USA.*

Inbred mice strains differ in their unconditioned preferences for caloric and oncaloric sweeteners due to allelic variations in the gene coding for the T1R3 sweet taste receptor. Confirming prior reports, naive 129P3/J (129) 'nontaster' mice were indifferent to sucrose solutions at low concentrations (0.5–2%) that C57BL/6J (B6) 'taster' mice preferred in 48 h sugar vs. water tests. Sucrose preference did not differ at 16% and 32% concentrations. After exposure to these concentrated solutions, the 129 and B6 mice showed identical robust preferences (>90%) for 0.5% to 32% sucrose, although 129 mice drank less sucrose (in grams) at dilute concentrations compared to B6 mice. Tests with descending sucrose concentrations revealed a similar preference threshold (0.0625%) in the two trains. 129 mice, but not B6 mice, then lost their preference for 0.5% sucrose with repeated 2-bottle testing (6 days). These results show that exposure to the taste or more likely the postingestive actions of concentrated sucrose conditions a strong preference for dilute sucrose solutions in 'nontaster' 129 mice. The preference 'extinguishes' with repeated testing. Whether the conditioned 129 mice responded to the taste or other properties (e.g. odor) of dilute sucrose is not certain. Sucrose-conditioned 129 mice also showed an enhanced preference for dilute saccharin solutions suggesting that their sweet taste responsivity was enhanced. Thus, the gustatory capabilities of 'nontaster' mice need to be reconsidered. In addition, the results of sweetener tests in mice with prior sugar experience should be interpreted with caution. Supported by NIH Grants DK-31135 and DK-59630.

Changes in ingestive pattern in blinded rats. BRAHIM SELMAOUI, JIM WATERHOUSE, LOUISE THIBAULT. [a]*Centre d'étude du sommeil et des rythmes biologiques, Laboratoire de chronobiologie, Hôpital du Sacré-Coeur de Montréal, Québec, Canada, H4J 1C5;* [b]*Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool, UK, L3 2ET, 3School of Dietetics and Human Nutrition, McGill University, Québec, Canada.*

Eating and drinking patterns were examined in intact and blinded adult male Sprague–Dawley rats fed a choice among isocaloric casein, sucrose/dextrin, and vegetable shortening/soybean oil diets. Weekly mean intake of all nutrients was altered in blinded rats, with increased lipid intake and decreased water intake in rats blinded for 2 weeks, lower carbohydrate but higher protein and water intakes in rats blinded for 4 weeks, while 2 weeks later blinded rats maintained high intakes of protein and water. The amplitudes of the daily rhythms for each nutrient behaved similarly to the weekly intakes. Delayed daily time of peak intake for all nutrients over successive weeks after blindness were found, indicating that the timing of peak intake free-runs. 24 h profile indicated time of day variations of nutrient intake tending to be less marked over successive weeks of blindness. Free-running animals maintained the link between carbohydrate intake and hypothalamus serotonin.

Dietary selection paradigm and its reliability for the nychthemeral intakes of water and macronutrients. B. SELMAOUI[a], J. PAQUET[a], L. THIBAULT[b]. [a]*Chronobiology Laboratory, Sacré-Cœur Hospital, Montreal, Canada;* [b]*School of Dietetics and Human Nutrition, McGill University, Canada, H9X 3V9.*

Rats with ad libitum water and the ability to self-select among three macronutrient-rich diets: carbohydrate (CHO), protein (PRO) and lipid (LIP), show a circadian rhythmicity in their ingestion. The aim of the present study was to determine whether this circadian rhythmicity is reliable from day to day. Eight rats were offered ad libitum water and a choice of three isocaloric diet rations providing carbohydrate, protein and lipid separately. Water and food intake was recorded every 3 h for 7 days. The reliability of the circadian rhythm of water and food intake was determined by the Intraclass correlation (ICC) and by the test-retest reliability by using the Pearson's correlation coefficient (*r*). The results showed that the circadian rhythm of water, CHO and PRO intake are strongly reliable. However, the circadian rhythm of LIP intake is less reproducible. Moreover, among the three reliable parameters: water, CHO and PRO, the circadian rhythm of water intake is the most reproducible over 7 days. This suggests that water intake may be used as a marker of circadian rhythmicity in ingestive behavior.

The orexigenic action of stimulating μ-opioid receptors (μOR) in the parabrachial nucleus (PBN) is associated with increased incorporation of guanosine-triphosphate-g-^{35}S (GTP-g-^{35}S) and c-fos translation. K.J. SIMANSKY, E.K. ENGLE, H.G. FROST, V.J. ALOYO, D.M. NICKLOUS. *Department of Pharmacology and Physiology, Drexel University College of Medicine, Philadelphia, PA.*

Infusing the μOR agonist DAMGO into the lateral parabrachial nucleus increases food intake in rats. The μOR antagonist CTAP inhibits this response. We analyzed the relationship between DAMGO-elicited eating and G-protein coupling in the PBN as measured by the incorporation of GTP-γ-^{35}S. In vitro, DAMGO dramatically increased GTP-γ-^{35}S labeling in the external lateral and central lateral subnuclei. Basal incorporation was 158 ± 22 nCi/g for the external lateral and 158 ± 12 nCi/g for the central lateral subnucleus. DAMGO (1 μM) increased this 100% to 316 ± 19 and 59% to 251 ± 10 nCi/g, respectively. Intense activation coincided with the densest concentration of μORs revealed by immunofluorescence. CTAP (100 nM) reduced DAMGO-stimulated binding to basal for the external lateral and near basal for the central lateral subnucleus. We also quantified the ability of DAMGO infusions to increase translation of c-fos in the lateral PBN in nondeprived rats. Virtually no c-fos immunoreactive cellular nuclei (c-fos-IR) were detected after infusing vehicle. In comparison, DAMGO increased c-fos markedly in the central parabrachial subregion (central, crescent, dorsal), much less in the external lateral region and minimally in the ventral subnucleus of the lateral PBN. CTAP reduced the c-fos response. Finally, parabrachial DAMGO also increased c-fos-IR in the ipsilateral shell of the nucleus accumbens. Together, these data suggest that cellular inhibition associated with activating μOR coupling in the PBN disinhibits an excitatory pathway for eating. Furthermore, a multisynaptic circuit originating in the PBN recruits forebrain regions involved in natural reward. Supported by NIH grant DK58669 to KJS.

Enhanced expression of the hypothalamic leptin receptor after repeated neurogenic stress. N. SIMLER, A. PEINNEQUIN, A.X. BIGARD. *Department of human factors, National Health Research Center for Defense, 38702 La Tronche, France.*

Neurogenic stress is known to markedly affect feeding behavior and energy stores. Compelling evidence suggest a link between dysfunction of the hypothalamic-pituitary-adrenocortical system and eating disorders associated with central leptin resistance. We hypothesized that repeated neurogenic stress may lead to diminished leptin sensitivity of the hypothalamus, either mediated by an inappropriate response of the neurons targeting leptin or by a disrupted response of the brain leptin receptor. We therefore examined the effects of repeated restraint on the expression of (1) the stress-induced hormone CRF, (2) the leptin responsive neuropeptides NPY and POMC, (3) the leptin receptor OB-Rb in the hypothalamus. Adult male Fisher-344 rats were subjected to one, two, or repeated restraint stresses (4 h each bout, 13 days for the repeated stresses). The paraventricular (PVN) and arcuate (ARC) hypothalamic nuclei were isolated from brain by bilateral punches and mRNA expression was assessed by real-time quantitative PCR. Restraint-stress induced an immediate transient drop in daily food intake (day 1 to 3), a persistent weight loss and decreasing circulating leptin levels beginning on day 2. Acute restraint increased first CRF mRNA in the PVN and NPY mRNA in ARC, then POMC mRNA in ARC after two sessions. After 13 days, all mRNA values had recovered their initial levels, while OB-Rb gene was markedly up-regulated (max 6 fold) in ARC throughout restraint-stress exposure. These data attest for an acute response of the anorexic factor CRF, and by an associated response of the orexigenic factor NPY. The increased expression of the brain leptin receptor after acute and repeated restraint suggests that neurogenic stress doesn't alter leptin signaling in the hypothalamus.

Attenuated feeding responses to circadian and palatability cues in mice lacking neuropeptide Y. D.K. SINDELAR, R.D. PALMITER, S.C. WOODS, M.W. SCHWARTZ. *Eli Lilly and Co, University of Cincinnati, University of Washington.*

While abundant evidence implicates neuropeptide Y (NPY, a potent orexigenic peptide) in the hypothalamic control of energy homeostasis, NPY-deficient (Npy − /−) mice consume normal amounts of food and gain weight normally, suggesting that NPY is not required for normal feeding behavior. The current studies were undertaken to test the hypothesis that NPY is a determinant of feeding in response to specific stimuli. For example, circadian cues have an important effect on food intake such that in normal mice, the maximal rate of food consumption occurs at the onset of the dark cycle. During the first 4 h after dark cycle onset, Npy − /− mice fed chow ad libitum consumed 33% less than did Npy + /+ controls (0.6 ± 0.1 g vs 0.9 ± 0.1 g; $P \leq 0.05$), whereas 24-h food intake was no different between genotypes (3.7 ± 0.2 g vs 3.5 ± 0.3 g; $P =$ ns). In contrast, 4 h intake at the onset of the dark cycle was identical between Npy − /− and Npy + /+ mice when measured following a 24 h fast (1.4 ± 0.1 g for both groups, $P =$ ns). This effect of fasting to normalize intake at dark cycle onset occurred despite a pronounced delay in the onset of feeding exhibited by NPY-deficient mice. Thus, the latency to initiate feeding was 4-fold greater in Npy − /− than control mice (636 ± 133 sec vs 162 ± 29 s; $P < 0.05$), despite no difference in the latency to investigate food (89 ± 13 vs. 90 ± 6 s; $P =$ ns). To investigate the effect of NPY deficiency on the response to palatability cues, mice were presented with a highly palatable diet (HP) for 1 h each day (in addition to ad libitum access to chow) for 18 days. Npy + /+ mice rapidly increased daily HP intake such that by the end of the first week, they derived a substantial fraction of daily energy from this source (41 ± 3%). In contrast, Npy − /− mice consumed much less HP (24 ± 7% of daily energy intake, $P \leq 0.05$ vs Npy + /+), although HP intake was eventually (by D9) comparable between genotypes. These experiments suggest a key role for NPY in the increase of food intake that occurs both at the onset of the dark cycle and in response to increased palatability of the diet.

Satiety and metabolic responses after modified sham feeding. J.P.G. SMEETS[a,b], M.S. WESTERTERP-PLANTENGA[a,b]. [a]*Maastrciht University, Department of Human Biology, P.O. Box 616, 6200 MD, Maastricht, The Netherlands;* [b]*Wageningen Centre for Food Sciences (WCFS), P.O. Box 557, 6700 AN, Wageningen, The Netherlands.*

We investigated cephalic and metabolic responses to oral stimulation using a high-fat meal in the postprandial phase. A cross-over design with 10 subjects (6 females and 4 males). Vagal stimulation was achieved by using the modified sham feeding (MSF) technique, in which nutrients are chewed and tasted but not swallowed. Five hours after a high-fat breakfast (59.4 g fat), the subjects were given 1 of 3 test meals in random order: a high-fat lunch (35.7 g fat), water or MSF (35.7 g fat). Blood was collected for 3 h after the test meal for metabolite analysis, and Visual Analog Scales on the appetite profile were completed. The delta area under the curve (deltaAUC) of hunger and appetite after MSF were higher than after feeding ($P < 0.05$), but did not differ significantly from water; there was no significant difference between feeding and water. The deltaAUC of satiety after MSF was lower than after feeding ($P < 0.05$), but did not differ from water. The change in blood glucose was not different between treatments. After feeding the deltaAUC non esterified fatty acids (NEFA) was larger than after water ($P < 0.05$); deltaAUC NEFA after MSF did not differ from feeding or water. The change in triacylglycerol (TAG) and glycerol was increased 60 min. after MSF compared to after water ($P < 0.05$). MSF seems to trigger metabolic responses and feelings of fullness similar to feeding. Yet, in contrast to feeding, MSF seems to stimulate appetite and reduce satiety.

Effect of short-chain acyl-CoA dehydrogenase (SCAD) deficiency on response to sucrose polysoyate oil in brief access taste tests. B.K. SMITH RICHARDS, B. YORK, B.N. BELTON, J. VOLAUFOVA. *Pennington Biomedical Research Center, LSU, Baton Rouge, LA, USA.*

A functional SCAD enzyme is absent in BALB/cByJ mice due to a spontaneous mutation in *Acads* (Wood et al., 1989). *Acads* −/− mice avoid fat and prefer carbohydrate in diet selection paradigms (Smith Richards et al., 2004). Based on the premise that fat preference or aversion is conditioned by postingestive effects of the nutrient, we hypothesized that SCAD deficiency would not effect taste responsiveness to oil emulsions during brief access tests using an automated lick sensor. Based on current literature, tests of 5 to 15-s duration are considered sufficiently short intervals for discriminating between the oral and postoral effects of a taste stimulus. In tests employing successive 15-s presentations of corn oil in an ascending concentration series ending with 50%, we observed previously that naïve *Acads* −/− mice licked significantly less of 50% corn oil than *Acads* +/+ mice did, suggesting the possible chemical detection of fat or other orosensory mechanism(s). To rule out the first possibility, we next tested taste responsiveness to a non-caloric fat substitute. Here we show that naïve *Acads* −/− mice licked significantly less of 50% sucrose polysoyate oil compared with *Acads* +/+. Real-time analyses (licks per s) revealed that this strain divergence occurred within 2 s of the initiation of licking. These results are consistent with evidence for a population of neurons in the primate orbitofrontal cortex that respond rapidly to oral texture of fat through the somatosensory system (Rolls et al., 1999). We propose that SCAD deficiency modifies the perception of corn and sucrose polysoyate oils through a somatosensory mechanism rather than a chemosensory one.

Otitis media and head trauma influence adult body mass: Separate and combined effects. D.J. SNYDER, V.B. DUFFY, A.K. CHAPO, L.M. BARTOSHUK. *Neuroscience and Surgery, Yale University School of Medicine, New Haven, CT, USA.*

Because the chorda tympani (VII) passes through the middle ear, diseases of the ear (i.e. childhood otitis media, OM) can alter taste perception. Oral sensation guides food choice and body mass index (BMI), and we have shown that male supertasters (ST) of PROP (6-n-propylthiouracil) over age 30 + with severe OM history have significantly elevated BMIs, presumably via disinhibition of oral tactile cues (i.e. fat perception) preferred by some ST men. Head trauma (HT) is a more general source of oral sensory damage, but its effect on dietary health remains unclear. Caucasian survey participants ($N = 2897$) assessed age, sex, OM and HT history, food preferences, and PROP intensity. A history of severe OM was linked to increased BMI in both men (especially STs) and women over age 30, supporting our view that OM produces incremental sensory change over time. By itself, HT interacted with sex, age, and PROP status to drive modest (albeit significant) BMI changes, perhaps reflecting broad sensory losses that selectively guide oral disinhibition. However, when combined with mild OM, HT potentiated BMI gain in ST men. Analyses of food preference are ongoing. Overall, men and women aged 30 + with OM history may be at high obesity risk due to VII damage. Male STs appear to be at special risk: Some prefer high-fat foods already, OM damage probably produces intense disinhibition of fat cues, and HT augments the impact of OM. (DC 00283)

The role of brain-derived neurotrophic factor (BDNF) in food intake and body weight regulation. A.D. STRADER, D.J. CLEGG, S.C. BENOIT, R.J. SEELEY. *Genome Research Institute, University of Cincinnati, Cincinnati, Ohio 45237.*

Brain-derived neurotrophic factor (BDNF) is a well known neurotrophin involved in the protection of neuronal degeneration within regions of the cortex and hippocampus. More recently BDNF has been added to the growing list of peptides and hormones that regulate food intake and energy balance. In support of this is the fact that BDNF neurons are present within important hypothalamic nuclei that regulate food intake and body weight. Previous data demonstrated that continuous (14 day) ventricular infusions of BDNF induce lasting body weight and food intake reductions in rats. In the present study three dose-response experiments were performed to investigate the effects of single third ventricular injection of BDNF on food intake and body weight. Interestingly, we determined that a single dose of 250 ng, lower than previously reported doses, reduced food intake for two days and caused significant weight loss. Reductions in food intake were not associated with illness and animals did not develop a conditioned taste aversion. Consistent with the prolonged anorexic effect, indirect calorimetry determined that BDNF-induced weight loss was the result of an increase in energy expenditure during both the dark and light phase. BDNF gene expression is also partially regulated by energy state as BDNF mRNA was reduced by 40% in the hypothalamus of rats fasted for 24 h. In contrast, hypothalamic BDNF mRNA was not affected by prolonged exposure to a high fat diet. In summary, BDNF reduces food intake without causing illness, increases energy expenditure, and gene expression is regulated by energy balance. These findings suggest that BDNF is directly involved in the regulation of food intake and energy homeostasis.

Rapid osmoregulation when rats consume high salt diet: the role of gastric chyme. E.M. STRICKER, J.G. SPICER, M.L. HOFFMANN. *Neuroscience, University of Pittsburg, Pennsylvania.*

Gastric emptying of ingested food proceeds similarly whether rats eat dry laboratory chow containing 1% or 8% NaCl. This observation is surprising because gastric emptying of hypertonic liquids is known to inhibit gastric emptying. Perhaps in explanation, the gastric chyme in rats fed either of the two diets is comparably dense (approximately 1 g food: 1.2 ml fluid). In other words, very high levels of salt in the chyme do not create an osmotic movement of water into the stomach. The dietary salt apparently cannot be detected until the chyme empties into the duodenum, whereupon increased water intake occurs periodically during a meal. The present experiment further examines these issues in rats after surgical removal of all salivary secretions. Such 'desalivated' rats drank large volumes of water during a meal in order to swallow the dry food, and they consumed even more water when food contained 8% NaCl instead of 1% NaCl. More to the point, calculations indicate that the amount of water consumed, when mixed with the NaCl content of the ingested high-salt food, would produce an isotonic saline solution. In fact, direct measurement of the gastric fluid confirmed this isotonicity. Note that a dense gastric chyme was not formed in their stomachs, and instead food particles were suspended in a large quantity of ingested liquid. These results indicate that the formation of a dense gastric chyme is adaptive in reducing the early osmotic consequences of eating high-salt diet. The results also suggest that in these animals visceral osmoreceptors detect the concentration of the fluid leaving the stomach and promptly stimulate osmoregulatory drinking.

Subjective arousal and mood affect people's eating behavior in the natural environment. N. STROEBELE, J.M. DE CASTRO. *Georgia State University, Food Intake Laboratory, Atlanta, GA.*

The presence of other people, the location of intake, and the time of consumption, have a significant impact on food intake. However, why more is eaten under these conditions is less clear. It was hypothesized that physiological or subjective arousal might play an important intermediary role. College students ($n = 77$) were instructed to maintain a detailed diary about their food intake including premeal subjective arousal and mood ratings for seven consecutive days. In addition, Polar Heart Rate Monitors were used to continuously record the participants' heart rates. No significant differences in mean heart rates or changes in heart rates were detected comparing different locations, amount of people or time of consumption. On the other hand subjective arousal was significantly associated with more people present as well as with consumption in restaurants. Furthermore, those situations were rated as more pleasant and the participants reported themselves to be more elated. Meals rated as more pleasant were significantly higher in fat and protein intake. The results suggest that heightened subjective arousal and mood are related to certain eating situations, while there is no relation between heart rate and situational variables. This supports the hypothesis that subjective arousal might mediate the influence of some environmental variables on food intake.

Interaction between circadian and energetic control of feeding behavior: Effect of ageing. J.H. STRUBBE, P. VAN DER VELDE, G. VAN DIJK. *Department of Neuroendocrinology, University of Groningen, P.O. Box 14, 9750 AA Haren, The Netherlands.*

In the rat the energy content is subject to homeostatic control achieved by adjustment of food intake. The regulation of feeding behavior, however, is not only mediated by signals reporting energy deficits. Also circadian rhythmicity plays a role. The present studies were undertaken to investigate the relative contribution of factors signaling the energy content of the body and circadian timing factors in determining the temporal distribution of feeding behavior. Rats have most food intake in the dark with peaks at the beginning and end. We observed that circadian factors play an important role in the causation of the peak at the end, whereas energetic regulation is important at other times. This was based on the following lines of evidence. Intragastric infusions of liquid food were less effective in suppressing food intake towards the end of the dark phase. In contrast infusions in the beginning of the dark phase caused a load-dependent postponement of the first meal. Aged rats that have a decreased expression of circadian rhythmicity were more sensitive to these gastric infusions. In addition the correlation between meal size and subsequent intermeal interval is stronger after lesioning of the circadian pacemakers in the suprachiasmatic nucleus (SCN), than in control rats. Together, these results indicate that under normal conditions circadian pacemaker activity strongly interacts with energy regulation, and that these interactions diminish during ageing.

CCK-induced activation of the MEK-ERK-CREB signaling-cascade in NTS neurons is modulated by melanocortinergic input. G.M. SUTTON, B. DUOS, L.M. PATTERSON, H.R. BERTHOUD. *Neurobiology of Nutrition Laboratory, Pennington Biomedical Research Center, Baton Rouge, Louisiana, USA.*

Neurons in the Nucleus Tractus Solitarius (NTS) are involved in the integration of visceral satiety signals through vagal afferent input and this is thought to govern direct control of food intake. We hypothesized that the hypothalamic melanocortin system modulates this brainstem process through the MAPK (ERK 1/2) signaling cascade. Using 4th ventricular cannulated rats, Western Blotting, and immunohistochemistry, we have previously shown that the visceral satiety signal CCK (2–100 μg/kg, i.p.), dose dependently increases phosphorylation of ERK 1/2 within minutes in specific NTS neurons. Here we show that the MC4-R agonist, MTII (0.05 and 0.2 nM, 4th V) dose-dependently increases phospho-ERK in the NTS within 30 min, and that a low dose of MTII (0.05 nM, 4th V) injected 30 min prior to a low dose of CCK (2 μg/kg, i.p.) resulted in an additive stimulatory effect on phospho-ERK. In contrast, prior treatment with the MC4-receptor antagonist SHU9119 (1 nM, 4th V) almost completely abolished CCK-induced (10 μg/kg, i.p.) increases in phospho-ERK. In an effort to identify the phenotype of NTS neurons involved, immunohistochemistry had previously shown that CCK stimulates phosphorylation of ERK1/2 in a fraction of NTS noradrenergic neurons, and we show here that CCK stimulates phosphorylation of tyrosine hydroxylase at the threonine-31 site. We conclude that the ERK-signaling cascade may act as an integrator for visceral satiety signals and longer-term hypothalamic signals mediated by descending melanocortin projections, and that some catecholaminergic neurons in the NTS may play a role in this mechanism. Supported by NIH DK47348.

Meal size control by converging visceral satiety signals and melanocortinergic inputs on MAPK (ERK1/2) signaling cascade in NTS neurons. G.M. SUTTON, B. DUOS, L.M. PATTERSON, H.R. BERTHOUD. *Neurobiology of Nutrition Laboratory, Pennington Biomedical Research Center, Baton Rouge, Louisiana, USA.*

Signals generated by gastric distension and CCK in the gut converge with signals from the hypothalamus and other higher brain areas in the caudal brainstem to orchestrate ingestive behavior and associated autonomic responses. We hypothesized that specific brainstem 'integrator' neurons in the dorsal vagal complex that receive input from CCK-activated vagal afferents are modulated by input from hypothalamic melanocortinergic neurons, and that the integrated signal determines the level of satiation and meal size. Since we previously showed that both i.p. CCK and 4th ventricular MTII dose-dependently stimulated phosphorylation of the MAPK (ERK1/2) in NTS neurons, we wanted to test whether activation of this intracellular signaling pathway is necessary for CCK's food intake suppressing effect. Prior treatment with the MEK inhibitor U0126 (2 μg, 4th V) significantly attenuated by 60% CCK's suppressive effect on food intake, without significantly changing basal (saline i.p.) food intake in overnight food deprived rats. In parallel, U0126 attenuated by 60% CCK-induced phosphorylation of ERK1/2 as assessed by Western blotting. In addition, CCK's stimulating effect on ERK1/2 signaling was enhanced by the MC4-receptor agonist MTII, and inhibited by the antagonist SHU9119 injected into the 4th V, and we found previously that 4th ventricular administration of these ligands modulates meal size in freely feeding rats. Together with the recently reported finding that CCK is unable to suppress food intake in MC4-receptor deficient mice, these results suggest that the ERK-signaling cascade in NTS neurons acts as an integrator of short and long-term satiety signals to determine meal size. Supported by NIH DK47348.

Enhanced glucose tolerance following recovery from social stress. K.L.K. TAMASHIRO[a,b], M.M.N. NGUYEN[a,b], L.Y. MA[b], D.A. D'ALESSIO[c], S.C. WOODS[b], R.R. SAKAI[b]. [a]*Neuroscience Program, University of Cincinnati Medical Center, Cincinnati, OH 45237-0506, USA;* [b]*Department of Psychiatry, University of Cincinnati Medical Center, Cincinnati, OH 45237-0506, USA;* [c]*Division of Endocrinology, University of Cincinnati Medical Center, Cincinnati, OH 45237-0506, USA*.

Male rats in mixed-gender rat colonies quickly form dominance hierarchies when housed in a visible burrow system (VBS), a laboratory model of chronic social stress. Subordinate (SUB) males consistently lose 10–15% of their original body weight over 14 days in the VBS, while dominant (DOM) males maintain or lose very little body weight. Body composition analysis showed that both DOM and SUB lost adipose tissue, but SUB lost lean tissue as well indicating that body composition changed during social stress. After 14 days in the VBS, SUB had elevated basal corticosterone and decreased testosterone suggesting that weight gain during a recovery period would be predominantly adipose tissue. When allowed to recover from VBS stress by 21 days of individual housing, SUB quickly regained lost body weight and were hyperphagic throughout the recovery period. Body composition analysis confirmed that SUB had a higher % body fat after the 21-day recovery period and this effect was further enhanced when rats were exposed to 2 cycles of VBS stress and recovery. Consistent with increased % fat, SUB also had elevated plasma leptin and fasted insulin levels suggesting that SUB were glucose intolerant. However, an oral glucose tolerance test after 21 days recovery showed that both SUB and DOM cleared a glucose load faster and with less insulin secretion compared to controls and this ability persisted after 42 days of recovery. These data suggest that increased physical activity in the VBS may enhance glucose tolerance in DOM and SUB. Supported by: NIDDK, NINDS, NARSAD, H.F. Guggenheim Foundation, Albert J. Ryan Foundation, and a University Research Council Fellowship.

Prolonged mild hyperglycemia: effect on cardiac vagal activity and food intake in humans. K.L. TEFF, M. PETROVA, R.R. TOWNSEND. *Monell Chemical Senses Center and University of Pennsylvania, Philadelphia, USA*.

The objectives of the present study were to determine how prolonged (48-h) elevations in blood glucose influence cardiac vagal activity, hormonal responses to ingested nutrients and food intake in human subjects. Lean men and women ($n = 14$) were tested under 2 randomized experimental conditions: (1) 48-h saline infusion (50 ml/h) and (2) 48-h glucose infusion (15% glucose; 200 mg/m2/min). Blood samples and blood pressure (BP) were taken every 2 h. Heart rate (HR) variability using a Holter Monitor was monitored continuously over the 48-h period. Food intake was measured during the 48-h period. Three hours after the infusion, subjects ingested a mixed nutrient meal (600 kcal) and blood samples taken. Mean 48-h glucose levels were 98 ± 6.4 mg/dl, saline compared with 113.5 ± 5.5 mg/dl, glucose ($P < 0.0001$). Mean insulin levels were 28.5 ± 5.7 μU/ml, saline compared with 57.3 ± 10 μU/ml, glucose ($P < 0.0001$). Mean plasma leptin levels were also significantly elevated after the glucose infusion (5.2 ± 3.6 ng/ml, saline vs. 7.5 ± 6 ng/ml, $P < 0.001$). Prolonged hyperglycemia decreased the night to day differences in heart rate variability (12.4 ± 12.2 ms, saline vs. 3.1 ± 10.0 ms, glucose $P < 0.03$), increased HR (61 ± 10 bpm, saline vs. 67 ± 7 bpm, glucose, $P < 0.05$) and systolic (BP)(107.5 ± 10.5 mmHg, saline vs. 113.9 ± 13.2 mmHg glucose, $P < 0.02$) on the second day of hyperglycemia. No significant differences in food intake or hunger ratings during the 48-h infusions were observed during the two treatments. Post-prandial insulin and glucose levels were significantly reduced following the glucose infusion compared to the saline. These data suggest that relatively mild, short-term increases in blood glucose can infuence cardiac vagal activity and hormonal responses to a meal but that 48-h is insufficient for caloric compensation to nutrient infusion to occur in humans.

Influence of genetic taste sensitivity to 6-*n*-propylthiouracil (PROP) and maternal variables on energy intake and adiposity in preadolescent children. B.J. TEPPER, G.L. GOLDSTEIN, H.L. DAUN. *Psychiatry, University of Wisconsin, Madison.*

Previous studies have shown that phenotypic differences in taste (as measured by screening for taste sensitivity to the bitter compound 6-*n*-propylthiouracil [PROP]) may be a marker for dietary behavior in children. Maternal disinhibition has also been identified as a critical determinant of food habits and adiposity in children. This study tested the hypothesis that non-taster status and disinhibition would be associated with higher energy intakes and body weights in children. Sixty-five children, 7–11 years of age and their mothers participated in the study. Energy and macronutrient intakes of children were estimated from 3-day food records. PROP status was determined using a paper disk method according to Zhao et al. (2003). Body mass index (BMI; kg/m^2) was determined in mothers and children. Maternal dietary restraint and disinhibition was measured with the 3-Factor Eating Questionnaire. Maternal disinhibition was associated with higher energy intakes in girls ($P < 0.01$). Non-taster children consumed more energy than medium or super-taster children and these differences were specific to girls ($P < 0.05$). There were no differences in macronutrient intakes or BMI as a function of PROP status among children. However, BMI was 6.2 units higher in non-taster mothers as compared to super-taster mothers ($P < 0.001$). Thus, current energy intakes were higher in non-taster girls as compared to taster girls, but differences in adiposity were not evident at this time. Our findings in mothers strongly suggest that PROP-related adiposity differences are likely to appear in these children later in their development. Together, these data suggest that genetic taste phenotype, gender, and maternal disinhibition exert complex influences on energy intakes and adiposity in preadolescents.

The Cannabinoid CB1 Receptor Antagonist SR141716A Reduces Ingestion Of A Fat Solution Through Changes In Motivational State. Zoë D. THORNTON-JONES[a], STEVEN P. VICKERS[b], PETER G. CLIFTON. [a]*Department of Psychology, Sussex University, BN1 9QG;* [b]*Vernalis Research Ltd., 613 Reading Road, Winnersh RG41 5UA.*

Previous reports have indicated that the cannabinoid CB1 receptor antagonist SR141716A induces hypophagia. Previous studies exploring the effects of cannabinoids on satiety and palatability have produced conflicting results. Therefore we explored the underlying behavioural mechanisms by examining the effects of SR1417161A (0, 0.3, 1, 3 mg/kg, i.p) on the microstructure of licking behaviour for a 10% Intralipid fat solution. The effects of SR141716A on bout size (number of licks in a bout) and the number of bouts were then compared to those obtained following two behavioural manipulations: modification of the palatability of the Intralipid by addition of quinine (0, 0.1, 0.4 mM) and variation in the animal's levels of motivation to drink by allowing access to the Intralipid prior to testing (0, 4, 8 min). SR141716A dose-dependently reduced ingestion of the Intralipid solution primarily via a decrease in the number of bouts and not via a reduction in bout size. Similarly decreases in the motivational state resulting from presatiation suppressed licking behaviour for Intralipid solely by reducing the number of bouts. In contrast, a reduction in the palatability of the Intralipid suppressed total intake exclusively due to a decrease in bout size. We conclude that SR141716A reduces licking behaviour for a fat solution in a manner consistent with an effect on motivational state, most likely by enhancing satiation. This study suggests a role for CB1 receptor activation in the motivational control of feeding behaviour.

Sodium preference and angiotensin-stimulated thirst in aged rats. R.L. THUNHORST, T.G. BELTZ, A.K. JOHNSON. *Departments of Psychology and Pharmacology and the Cardiovascular Center, University of Iowa, Iowa City, IA 52242-1407, USA.*

Aged rats have diminished thirst and salt appetite responses to homeostatic challenges involving loss of body fluids and electrolytes. We examined two possibilities for these behavioral deficiencies. First, we tested if old rats (20 mo) have altered preferences for saline solutions compared to young rats (4 mo) by using a standard test of sodium preference/aversion. The rats received an ascending series of NaCl concentrations (0.0–3.0%), then a descending series (1.4–0.0%), always in choice with distilled water. The resulting sodium preference/aversion curve suggests that old rats are as capable of tasting different sodium concentrations as young rats and have the same level of preference for sodium at most concentrations. Both ages prefer weakly hypotonic solutions and avoid strongly hypertonic solutions. Next, we tested water drinking in response to angiotensin II (Ang II) administered centrally. Ang II was injected into the lateral ventricle (0, 0.2, 2 and 20 ng) and intakes were recorded for 30 min. There were no differences in water drinking between young (5 mo) and old (30 mo) rats. These data suggest that diminished water drinking of old rats after renin-dependent thirst challenges is not likely due to reduced capabilities of the aging brain to respond directly to Ang II. In summary, reduced thirst and salt appetite responses of aged rats are not likely to reflect altered sodium preference or reduced sensitivity of central angiotensinergic systems. Other possibilities (e.g. impaired renin secretion, impaired sensing of arterial blood pressure/volume signals) should be considered.

Sex differences in the activation of the long form of the leptin receptor. E.G. TOLOD-RICHER, D.J. CLEGG, R.J. SEELEY, S.C. WOODS. *Department of Psychiatry, Obesity Research Center, University of Cincinnati, Cinicnnati, OH.*

The distribution of fat within the body varies between genders. On average, females store more fat in the subcutaneous depot and this is associated with relatively higher levels of leptin. Males, on the other hand, store more fat in the visceral depot and this is associated with relatively lower levels of circulating leptin. Associated with these different body-fat distributions, we have previously found significant sexual dimorphisms in the anorexic response to leptin, with females being significantly more sensitive to central leptin administration than males. The current study sought to determine whether the actions of leptin and its intracellular signaling cascade, could account for these differences in sensitivity. After leptin binds to its receptor, Ob-Rb, it increases Janus-kinase 2(JAK2) and signal transducer and activator of transcription 3 (STAT3) levels within the neuron. To assess this activation we used immunohistochemistry for the activated form of STAT3, i.e. phophorylated STAT3 or pSTAT3. Higher staining for pSTAT3 should be associated with increased leptin action. Our preliminary data suggests leptin administered I3VT to intact females produces greater levels of pSTAT-like immunoreactivity in the arcuate (ARC) nucleus of the hypothalamus than in males. Furthermore, leptin-injected ovarectiomized females had lower pSTAT-like immunoreactivity in the ARC than intact females. These results suggest that differential sensitivity to the anorectic actions of leptin in males and females is associated with differential ability to induce pSTAT in the arcuate nucleus.

Determinants affecting physical activity in animal models: an overview. J. TOU, C. WADE. *Wyle Research Laboratories, NASA Ames Research Center, Moffett Field, CA, USA.*

Reduced energy expenditure is a major underlying cause in the increased prevalence of weight gain and obesity. In our sedentary environment, it is important to determine the parameters affecting physical activity. We provide an overview of various determinants involved in the regulation of physical activity. The role of genetics, hypothalamic injury, age and gender are briefly discussed with results from representative studies. Focusing on diet as a determinant of physical activity, differences in the levels of the dietary components fat and sucrose had no impact on activity. However, food-depriving rats resulted in increased activity indicated by measurement of higher locomotor activity. Comparison of locomotor activity in food-deprived obese, lean and control rats indicated hyperactivity occurred upon attaining a critical weight loss. The results suggested that body weight plays an underlying role in the regulation of activity. An inverse correlation ($r = 0.75$) between body weight and activity between different mice strains of genetically obese mice support a weight–activity relationship. To overcome challenges associated with establishing a weight–activity relationship, we use the novel tool of centrifugation. Altering gravity changes body weight based on knowledge that body weight is a product of the animal's body mass and gravity field to which it is exposed. Additionally, we propose the importance of considering the contribution of non-exercise activity thermogenesis (NEAT), the energy cost of all non-volitional activity, i.e. fidgeting, in the interpretation of results of activity studies. Better understanding of the importance of determinants affecting physical activity is essential for the development of strategies for the prevention of weight gain and obesity in the population.

Genetic loci related to bone and body composition identified by genotype–phenotype association of 40 inbred mouse strains. M.G. TORDOFF, S.A. DOMAN, E.A. BYERLY, D.M. PILCHAK, A.A. BACHMANOV, D.R. REED. *Monell Chemical Senses Center, Philadelphia, PA 19104, USA.*

To identify some genetic loci underlying bone and body composition, we compared phenotypic data obtained from a screen of body composition (see accompanying abstract) with SSLP marker allele sizes for 40 strains of mice. We combined two publicly available databases (CIDR and MPD) to obtain allele sizes at a total of 689 markers with an average of 557 markers per strain (range, 269–670) and between 2 and 13 different allele sizes per marker. To assess the involvement of a particular locus, mean strain values for each dependent variable were collated according to allele size and then analyzed by unweighted means ANOVA. Using a conservative criterion for significance ($P < 0.001$), there were differences related to allele size at 2 loci for bone mineral density, 21 loci for bone mineral content, 38 loci for carcass lean weight, 86 loci for carcass fat weight, 66 loci for total body weight, and 31 loci for percent of carcass as fat. Some of these loci correspond to QTLs determined by genetic analysis of segregating hybrids. Despite several caveats, this approach appears to be a simple first step to identify candidate genetic loci contributing to particular traits. It also identifies strains that are likely to be useful for more conventional genetic mapping studies.

Pairing nutrient infusions in the duodenum with malaise ('intestinal taste aversion' paradigm) alters oral intake and selection of nutrients. A.L. TRACY, R.J. PHILLIPS, M.M. CHI, T.L. POWLEY, T.L. DAVIDSON. *Department of Psychological Sciences, Purdue University, West Lafayette, IN, USA*.

We have previously reported that rats are capable of differentiating gastric infusions of fat and carbohydrate. This was demonstrated by separately infusing a Polycose solution (100% carbohydrate calories) or an equicaloric corn oil emulsion (100% fat calories) and pairing one of these nutrient infusions with malaise (i.p. LiCl). The fat and carbohydrate solutions were then presented simultaneously for an oral choice test. Although the animals had never previously consumed these solutions, their intake of the poisoned (i.e. LiCl-paired) nutrient was significantly lower than that of the non-poisoned (i.e. saline-paired) nutrient. We suggest that this reflects a mechanism by which rats can translate stimulation of the GI tract by these nutrients into an orally detected taste. This translation allows them to select between these nutritive solutions based on previous associations between the 'taste' as detected in the gut and associated post-oral stimuli (i.e. the LiCl-induced malaise). Here, we present experiments designed to further explore this phenomenon. The experiment described above was repeated using duodenal, rather than gastric, nutrient infusions in an attempt to assess the level of the GI tract at which the relevant components of these stimuli are being detected. Associating malaise with duodenal infusions replicated the effects observed with gastric infusions on oral intake and selection, thus implicating the intestines as the locus of the chemoreception and suggesting that reflux cannot account for these results. Additional findings obtained using this 'intestinal taste aversion' paradigm to further explore the phenomenon will be discussed. Supported by NIH R01HD29792 (TLD), R01DK27627 (TLP), R01DK61317 (TLP and RJP) and an NSF Graduate Research Fellowship (ALT).

NMDA channel control of meal size via central vagal afferent terminals. B.R. TREECE, R.C. RITTER, G.A. BURNS. *Programs in Neuroscience, Washington State University, Pullman, WA 99164-6520, USA*.

The NMDA ion channel blocker, MK-801, administered systemically or as a nanoliter injection into the solitary nucleus (NTS), increases meal size. MK-801 also attenuates reduction of food intake by cholecystokinin. Central vagal afferent terminals express NMDA channels, and we found that intra-nodose NMDA injection reduces NTS CCK binding. These results suggest that NMDA channels on vagal afferents may participate in MK-801 induced increase in food intake. We also found that MK-801-induced increases in intake are not abolished by subdiaphragmatic vagotomy. Therefore, we hypothesized that NMDA channel blockade at central vagal afferent terminals, which survive subdiaphragmatic vagotomy, might mediate increased food intake. To evaluate this hypothesis, we examined 30 min intake of 15% sucrose after 30 nl MK-801 injections ipsilateral or contralateral to a unilateral nodose ganglionectomy. Infusions of MK-801 on the side contralateral to ganglionectomy would reach intact vagal afferent terminals, while afferent terminals would be absent ipsilateral to ganglionectomy. Three additional control preparations also were included: sham ganglionectomy and sub-nodose vagotomy either contralateral or ipsilateral to NTS cannula placement. We found that rats with sub-nodose vagotomies increased their sucrose intake following MK-801, regardless of whether injections were made contralateral or ipsilateral to vagotomy. Rats with NTS cannula placements contralateral to nodose ganglionectomy also increased their intake following MK-801. However, rats with placements ipsilateral to ganglionectomy did not respond to MK-801. We conclude that central vagal afferent terminals are necessary for increased food in response to NMDA ion channel blockade. The function of central vagal afferent processes may be modulated by NMDA ion channels to control of meal size. Supported by DK 52849.

Modulation of gastric distension by CCK occurs via capsaicin-insensitive vagal afferents. E.H.E.M. VAN DE WALL[#], P. DUFFY, R.C. RITTER. *University of Groningen, Haren, The Netherlands. Washington State University, Pullman, USA.*

Capsaicin-treatment destroys vagal afferent C-fibers and markedly attenuates and induction of hindbrain Fos by cholecystokinin (CCK). However, both anatomical and electrophysiological data indicate that a majority of gastric afferents are not destroyed by capsaicin. Recently, Simasko et al. reported that CCK excites both capsaicin-sensitive C-type neurons, and capsaicin-insensitive A-type neurons in culture. Taken together, these results suggest that CCK might modulate responses to gastric distension via an action on capsaicin-insensitive afferents. To test this hypothesis we quantified expression of Fos-like immunoreactivity (Fos) in the dorsal vagal complex of capsaicin-treated (CAP) and control rats (VEH), following gastric balloon distension alone and in combination with CCK injection. In VEH rats IP CCK induced marked increase in Fos in the dorsal vagal complex, especially in nucleus of the solitary tract (NTS), while in CAP rats CCK did not induce significant increase in Fos. Both VEH and CAP rats exhibited distension-induced increases in Fos in the NTS. CCK significantly enhanced NTS Fos expression in response to gastric distension. Furthermore, CCK's enhancement of distension-induced Fos was especially evident in CAP rats, even though this group did not exhibit any significant increase in Fos after CCK alone. We conclude that CCK directly activates capsaicin-sensitive C-type vagal afferents. However, in capsaicin-resistant A-type afferents CCK may act by modulating responses to gastric distension. Thus, ingestive and gastrointestinal responses to CCK may be mediated through distinct actions of the peptide on afferent neurons with two different physiological phenotypes. This work was supported by grant number NS20561 to RCR, and by funding from NWO, BCN, Nicolaas Mulerius fund, the Netherlands.

Melanocortin receptors mediate CRH-induced neuroendocrine and thermogenic responses. G. VAN DIJK, K. DE VRIES, B.P. DEN HARTOG, C. NYAKAS, A.J.W. SCHEURINK. *Unit Neuroendocrinology, Department of Animal Physiology, University of Groningen, PO Box 14, 9750 AA HAREN, The Netherlands and cBrain Physiology Research Group of Hungarian Academy of Sciences, Semmelweis University, Budapest, Hungary.*

Evidence is accumulating that brain melanocortin receptors (MC-R's) are involved in leptin effects on food intake, neuroendocrine outflow and metabolism. Among the neurons down-stream from MC-R's are those containing corticotrophin-releasing hormone (CRH), with their cell bodies located in paraventricular hypothalamic nuclei. There are however also data suggesting the involvement of MC-R's in some CRH-mediated effects. To investigate a possible role of MC-R's in effects of CRH on HPA axis activity, thermogenesis, and food intake, rats were chronically infused into the third cerebral ventricle (i3cv) with SHU9119 (an MC3/4-R antagonist, 0.5 nmol/day) over a period of 14 days. When rats had relatively stable intake, they were injected via canulas located in the lateral cerebral ventricle (ilcv) with CRH (1.0 μg) or saline. Because i3cv SHU9119 treatment causes obesity, this study was also performed in i3cv SHU9119-treated rats that were pair-fed to saline-treated controls. This study revealed that anorexigenic effects of ilcv CRH were not impaired by i3cv SHU9119-treatment (but in fact, were amplified), but the ilcv CRH-induced increases in plasma ACTH and thermogenesis were markedly attenuated. Since the effects of MC-R blockade on the CRH-induced neuroendocrine and thermogenic responses could not be attributed to increased glucorticoid feedback (by assessing residual responses of ilcv CRH after ilcv or peripheral dexamethasone pretreatment), it may be proposed that MC-R's are located on terminals of CRH containing neurons in CNS areas involved in HPA axis activity (median eminence) and thermogenesis (brain stem and spinal cord), but not in areas involved in regulation of food intake.

Exercise and the brain: what do we know? J. VAN HOOMISSEN. *Department of Biology, University of Portland, Portland, OR, USA.*

Acute and chronic physical activity influence brain function, resulting in alterations in neuronal parameters such as brain morphology, neuronal firing rates, cellular metabolism, neurotransmitter concentrations and release, as well as influencing the number and sensitivity of receptors and the level of gene transcription and protein production. Investigations are now underway to determine how these changes in the structure and function of the brain after physical activity translate to alterations in behavior. The purpose of this talk will be to summarize the effects of physical activity on neural systems involved in modulating specific behaviors, such as ingestion.

Decreased sweet solution preference in dietary obese Sprague–Dawley rats. J.R. VASSELLI, C.D. COIRO, P.J. CURRIE. *Obesity Research Center, St. Luke's-Roosevelt Hospital, and Barnard College, Columbia University, NY, USA*.

Background: Leptin receptors are localized in the circumvallate papilla of the tongue, and act to suppress sweet taste stimulation (Kawai, PNAS, V97, 2000). Loss of this function in leptin receptor-mutant db/db mice results in enhanced sweet solution preference in 48 h two bottle preference tests for sugar solutions vs. water. Leptin receptor function is also impaired in obese wild-type rats in states of leptin resistance. *Design*: To test whether wild-type rats with leptin resistance also display enhanced sweet preference, groups of adult female S-D rats were fed either chow (CH) or high-fat diet (HF, 60% fat cal) for 24 weeks. To avoid taste contrast effects, the HF group was then switched to CH for 12 more weeks. Groups were then given ad lib access to 2 solutions (water vs. test solution) plus CH for 48-h intervals, with the solutions switched at 24 h. In the first test sequence, 8 saccharin concentrations (0.05–60 mM) were tested in ascending order, while in the second sequence, 9 sucrose concentrations (0.01–2.0 M) were tested. *Results*: The body weights and leptin levels of obese HF rats remained significantly elevated on CH. Obese rats showed significantly decreased preferences for all saccharin concentrations ($P < 0.05$ or smaller) except the two highest (48 and 60 mM, ns). Similar results were obtained with sucrose ($P < 0.05$). *Conclusions*: Results indicate that dietary obese rats, unlike leptin receptor mutant db/db mice, have decreased sweet solution preference, despite leptin levels indicative of central leptin resistance. Our data suggest that peripheral leptin receptors do not become resistant at elevated levels of the hormone.

Meal patterns of melanocortin receptor knockout mice using a simulated foraging protocol. C.H. VAUGHAN#, C. HASKELL-LUEVANO, N.E. ROWLAND. *Departments of Psychology and Medicinal Chemistry, University of Florida, Gainesville, FL 32611-2250, USA*.

We investigated meal strategies of mice as a function of cost for food. In our protocol, mice lived in a two lever operant chamber; completion of a designated number of responses (termed procurement cost or PFR) on the 'foraging' lever activated the other lever. On this second lever, completion of a designated number of responses (termed consumatory cost or CFR) produced delivery of a 20 mg food pellet. Animals could complete as many CFRs as they wished to form a meal. However, when 10 min elapsed without pressing this second lever, the meal was terminated and the foraging lever was again activated. In previous work with C57BL/6J mice (Vaughan & Rowland, 2003), we observed high meal frequency at low PFRs (10–30) and low meal frequency at the highest PFR (480). The present work applies this protocol to mice with deletion of either the melanocortin type 3 or 4 receptor (MC3RX-Merck Co.; MC4RX-Millenium Pharmaceuticals) compared with wild type (WT: a 129Sv-C57BL cross). Mice were run for ~1 week at each of six PFR-CFR schedules. Between each schedule, mice were given free food for ~3 weeks. At low PFR-CFRs (5-5, 15-5, 60-10), mice of all three genotypes took 6–8 meals/day of ~35 pellets/meal. At the highest PFR-CFR (480-10), all three groups consumed ~25% less than during other phases, and took 2–3 meals of ~60 pellets/meal. MC4RX were obese (44 ± 9 g) compared with WT or MC3RX (27 ± 6 and 26 ± 5 g, respectively), but were not hyperphagic in the experimental phases. Thus, while these mice showed well-defined changes in meal taking strategy as a function of imposed procurement cost, these adjustments are not dependent on either MC3 or MC4 receptors.

Predictors of weight regain after weight loss. N. VOGELS, M.S. WESTERTERP-PLANTENGA. *Department of Human Biology, Maastricht University, PO Box 616, 6200 MD Maastricht, The Netherlands*.

The purpose of the present study was to evaluate available variables of a long-term weight maintenance study, to investigate possible factors predisposing to weight regain after a period of weight loss. The Maastricht Weight Maintenance Study is an ongoing longitudinal study of healthy men and women (29 m/62f; 18–64 yrs; BMI 30.2 ± 3.1 kg/m^2). Different parameters were measured before and after a very low energy diet and after a follow-up of at least 2 years. Total body weight (BW) loss of the whole group was 7.9 ± 3.6 kg, and % weight regain (%WR) 113.8 ± 98.1%. In women %WR was correlated positively with the magnitude of change in body weight (amplitude of BW) ($r = 0.55$, $P < 0.001$). %WR was correlated negatively with resting metabolic rate (RMR) ($r = 0.55$, $P < 0.01$), but the correlation disappeared when RMR was corrected for fat free mass (FFM), indicating that FFM also played a role. Moreover absolute weight regain was positively correlated with the amplitude of BW (found in men ànd women) as well as with the frequency of dieting. The other measured variables at baseline (age, BMI, waist circumference, dietary restraint and respiratory quotient) did not contribute to the explanation of the variation in %WR. We conclude that the amplitude of BW and the frequency of dieting were the main predictors for weight regain. 55% of the variation in weight regain over a follow up period of at least 2 yrs was explained by the amplitude of BW, indicating a risk factor for women to become obese.

Subject specific treatment of obesity. N. VOGELS, M.S. WESTERTERP-PLANTENGA. *Maastricht University, Department of Human Biology, PO Box 616, 6200 MD Maastricht, The Netherlands*.

We investigated the effect of a subject specific treatment on weight maintenance in overweight and obese subjects, after a very low calorie diet (VLCD). One hundred and sixty nine subjects (BMI 31.1 ± 3.7 kg/m^2, age 48.1 ± 9.5 yr), followed a VLCD (2.1 MJ/d) for 6 weeks in a free-living situation, followed by a period of 1 year follow up. Subjects were measured right before (t0) and after (t1) the VLCD, after 3 months (t2) and after 1 year (t3). During the follow-up period, subjects were divided into four categories of weight maintenance advices (diet, activity, diet + activity, placebo), taking their compliance measured during weight loss and asked preference into account. Body weight (BW) loss during VLCD was 7.0 ± 3.1 kg. After 1 year follow-up weight regain was 56.3 ± 55.0%, without significant differences between the 4 advice groups. With respect to compliance during weight loss subjects with an increased dietary restraint had less BW regain than subjects with an increased physical activity (Baecke questionnaire) (35.5 ± 53.2 vs. 68.5 ± 46.4%, $P < 0.05$). Moreover, in these groups activity advices promoted weight maintenance (WM) in diet compliant subjects (%regain: 25.2 vs. 74.3%, $P < 0.05$). Subjects receiving an advice opposite to their preference showed a better WM than subjects receiving a preferred advice. We conclude that diet compliant subjects showed a better WM after weight loss, especially with additional activity advices. Subjects receiving advices opposite of their preference had less regain than people receiving preferred advices. New, unknown advices may have given subjects 'renewed' ideas on how to maintain their lower body weight.

Body mass index (BMI) and marijuana use. M.W. WARREN, K. FROST-PINEDA, M.S. GOLD. *College of Medicine, University of Florida*.

Substance abuse and overeating are leading causes of morbidity and mortality in the US. We have reported striking similarities between eating, overeating and addiction. Endogenous cannabinoid systems are believed to affect appetite and cannabinoid receptor agonists have been demonstrated to induce hyperphagia. Alternately, we have hypothesized and presented preliminary evidence that overeating may be a protective factor; reducing drug reward, addiction and relapse. In our previous studies, at higher BMIs alcohol use declined. Even though marijuana has been reported to stimulate appetite, we were curious if there was a similar tendency for the obese to have less marijuana use. As a follow-up, we examined charts of all females referred for morbid obesity/weight management in a 12-month period. Demographic, BMI and substance use data were collected from 297 charts. Results: Mean age was 40.6 ± 11.64 years (range, 16–79). Mean BMI was 46.1 ± 11.8 kg/m^2 (range, 27–107). Analysis was done to compare four groups. We found an inverse relationship between BMI and marijuana use. While 29% of the sample with BMI <29 ($n = 7$) used marijuana in the past year, only 21% of those with BMI 30–39 ($n = 84$), 16% of those with BMI 40–49 ($n = 110$) and 14% ($n = 96$) of those with BMI > 50 used marijuana in the past year. Because a linear relationship was observed, the linear term was tested using linear least squares regression. Indeed, linear regression revealed a negative correlation between BMI group and percent marijuana use (R-squared $= 0.96$; $P = 0.0173$). These findings provide support for overeating as competition for drugs and alcohol in brain reward sites. It also suggests that the regulation of appetite through the cannabinoid system may be dysfunctional in obese individuals.

The postingestive inhibitory effect of peptone emerges in rats between postnatal days 13–18. A. WELLER[a,b], L. TSITOLOVSKYA[a], G.P. SMITH[c]. [a]*Department of Psychology;* [b]*Gonda Brain Res Ctr, Bar-Ilan Univ, Ramat Gan, Israel;* [c]*Bourne Lab, Department of Psychiatry, NY-Presbyterian Hosp-Cornell Univ Med Coll, White Plains, NY, USA*.

Development of postingestive inhibitory control of intake by protein digestion products was investigated by administering gastric preloads of a meat hydrolysate peptone that decreased intake in adult rats (Schwartz et al., AJP, 276: R1623-1629 & 277: R1144-1151, 1999). Gastric preloads of saline or peptone, or sham preloads were given 5 min before a 30-min, independent ingestion test. Preloads of isotonic peptone reduced intake significantly more than preloads of isotonic saline on postnatal day (P) 18, but not on P12. Pretreatment with the CCK_A receptor antagonist devazepide (600 μg/kg, ip) did not change the inhibitory effect of isotonic peptone. Thus, the inhibitory effect of peptone on P18 was apparently not mediated by endogenous CCK acting at CCK_A receptors. In contrast to isotonic peptone, preloads of hypertonic peptone did not decrease intake more than preloads of hypertonic saline on P 12, 18, or 24. We conclude that if the isotonic peptone used in these experiments is an adequate model of the digestion products of dietary protein at these postnatal ages, then the postingestive inhibitory control of intake by digestion products of dietary protein during independent ingestion appears between P13 and P18.

Supported by the US-Israel Binational Science Foundation and the Rich Center, Bar-Ilan University.

Oral and gastro-intestinal satiety effects of capsaicine on food intake. M.S. WESTERTERP-PLANTENGA, A.SMEETS, M.P.G. LEJEUNE. *Department of Human Biology, Maastricht University, Maastricht, The Netherlands.*

Capsaicine, being the pungent principle of red pepper, has been shown to reduce food intake and increase fat-oxidation. We therefore examined the relative oral and gastro-intestinal contribution to capsaicine induced satiety and effects on food intake or macronutrient selection. From 24 subjects (12 men and 12 women; age: 35 ± 10 yrs; BMI: 25.0 ± 2.4 kg/m^2; range 20–30) 16 h food intake was assessed four times during 2 days by offering macronutrient specific buffets and boxes with snacks, in our laboratory restaurant. Thirty minutes before each meal 0.9 g (80,000 Scoville Thermal Units) capsaicine or placebo was offered in either tomato-juice or two capsules. Hunger and satiey were scored using Visual Analogue Scales. Average daily energy intake over 2 days in the placebo condition was 11.5 ± 1.8 MJ in the men and 9.4 ± 1.2 MJ in the women. After capsaicine ingestion in capsules this was 10.4 ± 1.6 and 8.3 ± 1.1 MJ ($P < 0.01$); after capsaicine ingestion in tomato juice 9.9 ± 1.4 and 7.9 ± 1.0 MJ, respectively (compared to placebo: $P < 0.001$; compared to capsaicine in capsules, corrected for energy content: $P < 0.05$). In both capsaicine conditions, en% from carbohydrate/protein/fat (C/P/F): changed from 46 ± 3/15 ± 1/39 ± 2 (en%) to C/P/F: 52 ± 4/15 ± 1/33 ± 2 en% ($P < 0.01$) in the men, and from C/P/F: 48 ± 4/14 ± 2/38 ± 3 en% to 42 ± 4/14 ± 2/32 ± 3 en% ($P < 0.01$) in the women; satiety (Area Under Curve) increased from 689 to 757 mmh in the men and from 712 to 806 mmh in the women, both ($P < 0.01$). We conclude that on the short term oral as well as gastro-intestinal exposure to capsaicine increased satiety and reduced energy and fat-intake over 24 h. However, with oral exposure reduction in energy intake was stronger, indicating a sensory effect on satiety.

Analysis of energy density effects from food and drinks separately on average daily energy intake. M.S. WESTERTERP-PLANTENGA, A.H.C. GORIS, K.R. WESTERTERP. *Department of Human Biology, Maastricht University, Maastricht, The Netherlands.*

Energy density only affects average daily energy intake if energy density is determined by the macronutrients and not if it is determined by water alone. Here we assessed the effect of variation in energy density (ED) of consumed foods and fluids on energy intake. Sixteen dieticians (age: 34 ± 9 yrs; BMI: 22.1 ± 2.3 kg/m^2) monitored intake twice, over 1 week, using weighed food records. Their recording of energy intake was accurate, according to water turnover using deuterium elimination; however they lost weight by under-eating. After feedback, the second time no under-eating or under-recording occurred. The latter intake data were analysed for energy density effects separately for food and drinks, on energy intake. Food was defined as all spoonable semi-fluids and solids. Drinks were defined as all drinkable liquids. From total energy intake (9.4 ± 1.4 MJ), 8.2 ± 1.2 MJ was from food and 1.2 ± 0.3 MJ from drinks. The energy density of the food was 6.5 ± 1.0 kJ/g; and of the drinks 0.7 ± 0.2 kJ/g. Total energy density was 3.1 ± 0.6 kJ/g. Energy density from both food and drinks contributed to total energy density ($r = 0.85$), partial $F = 43.8$ ($P < 0.0001$) for ED from food, and partial $F = 46.0$ ($P < 0.0001$) for ED from drinks. However, when assessing effects on total energy intake, only the energy density of food ($r = 0.47$; $P < 0.001$), and not the energy density from drinks contributed significantly to this. Thus energy density of food and not energy density of drinks is an important determinant of average daily energy intake.

Effects of leptin infusion in rats receiving either a self-selecting or a standard diet on food intake and body weight. S. WETZLER, G. JEAN-JOSEPH, D. TOME, C. LARUE-ACHAGIOTIS. *Unit INRA/INAPG 914 Nutr Physiol & Feeding Behavior, F75231 Paris cedex 05, France.*

The ability of leptin to alter food intake and reduced body weight gain (BWG) is now well established. Two groups of male rats were adapted during 2 weeks either to a self-selecting diet (Protein, carbohydrate (CHO), fat) or to a standard diet (14% protein, 72% CHO and 4% fat). Then, osmotic minipumps (7 days) containing leptin (1 mg/kg/day) or saline (control) were intraperitoneally implanted. Food intakes and BW were weighed every day. During basal period, standard-diet group (ST) had a higher energy intake (93.9 ± 2.3 vs. 68.6 ± 4.4 kcal) and higher daily BWG than self-selecting group (SS). They had the same BW at time of minipump implantation (215 g in average). Thereafter, ST leptin-treated group decreased significantly its total energy intake (−12%); in SS group, leptin infusion reduced total energy intake (−20%), by affecting mainly protein (−27%) and CHO intakes (−35.6%) with no difference regarding fat. BWG was higher in saline ST rats: 59.3 ± 2.1 vs. SS: 26.4 ± 2.3 g, while BWG was significantly reduced in leptin groups (ST: 46.8 ± 2.2 g vs. in SS 22.4 ± 2.4 g). ST rats had a significant higher WAT mass but leptin reduced it by 21% in both ST and SS rats; carcass weights (skeleton + muscle) were identical in all groups. Thus, as already observed, 1-ST induced a higher BWG affecting only WAT mass possibly due to elevated CHO intake; 2-chronic IP leptin reduced BWG and food intake in the same way in the 2 goups. It could be hypothesized that a higher dose of leptin would be necessary in ST rats in order to reduced more food intake.

Metabolic responses to ICV leptin injection in fed and fasted rats. S. WETZLER, S. DARE, C. LARUE-ACHAGIOTIS, D. TOME, P.C. EVEN. *Unit INRA/INAPG 914 Nutr Physiol & Feeding Behavior, F75231 Paris cedex 05, France.*

The effects of leptin on energy expenditure (EE) is still not well described and may change according to the feeding status of the rat. The aim of this study was to examine the acute effects of central leptin on the various components of total energy expenditure (total, resting and activity related energy expenditure (REE, TEE and AEE)), and respiratory quotient (RQ) measured with indirect calorimetry. ICV cannulated rats were injected with either leptin (5 μg/5 μl) or vehicle (5 μl) at the beginning of the dark phase and were allotted a 6 g calibrated meal of their standard diet (representing the spontaneous night food intake of leptin-treated rats, previous study) or were food deprived. Leptin injection increased REE in fasted but not in fed rats. This increase occurred without parallel changes in RQ, indicating that it resulted from an increase in both carbohydrate and lipid oxidation. Fasting induced an increase in AEE in vehicle-treated rats that was prevented by leptin treatment. In contrast, leptin-treated fed rats tended to be more active that vehicle-treated fed ones. It is concluded that the effects of leptin on energy metabolism depend on the nutritional status of the rats, with leptin poorly affecting the EE in the fed state, but increasing REE and decreasing AEE in fasted ones. These observations do not explain the reported decrease in meal size in leptin treated rats on an energetic base, but suggest that the intermeal interval in leptin rats may be preserved despite the decreased meal size by slowing down the decrease in REE and thus delaying the occurrence of hunger during transition from the fed to the fasted state (ischymetric hypothesis).

Sympathetic neurons are not required for either central or peripheral leptin-induced reductions in food intake or body weight. M.F. WIATER, S. RITTER. *Programs in Neuroscience, Washington State University, Pullman, WA 99164-6520.*

Female Sprague–Dawley rats were sympathectomized by neonatal guanethidine treatment or treated with saline. As adults, half of the rats in each group were injected with leptin. Peripheral leptin (20 mg/kg/day ip) reduced body weight significantly in both sympathectomized rats ($-7.4 \pm 0.7\%$) and controls ($-6.1 \pm 1.0\%$), but the amount did not differ between groups. After five days of peripheral leptin, food intake was significantly decreased from baseline to $60.3 \pm 4.6\%$ for controls and to $51.8 \pm 4.7\%$ for sympathectomized rats. After central leptin (2.5 mg/day, lateral ventricle), body weight was significantly decreased in both control rats ($-7.7 \pm 0.8\%$) and sympathectomized rats ($-5.9 \pm 0.9\%$)and the amount of weight loss did not differ significantly between groups. Likewise, food intake was significantly decreased in both control rats ($67.3 \pm 5.5\%$) and sympathectomized rats ($62.3 \pm 4.5\%$). After both peripheral and central leptin weight loss was primarily due to the decreased weight of metabolic white adipose tissue. Peripheral and central leptin reduce body weight and food intake similarly. Since both peripheral and central leptin activate central metabolic pathways, the primary site of leptin action appears to be central and not peripheral, and does not require sympathetic neurons, which were destroyed by guanethidine.

Gender specific adaptations in energy balance following implantation of artificial weight loads in mice. P. WIEDMER[a], M. BOSCHMANN[b], S. KLAUS[a]. *[a]German Institute of Human Nutrition Potsdam-Rehbruecke, Germany; [b]Franz-Volhard Clinical Research Center, Charité, Humboldt University Berlin, Germany.*

We recently showed that an artificial increase in body mass by implantation of metal weight loads for 3 months resulted in a compensatory decrease in body fat mass of male, but not female, wild-type mice. To further characterize this effect, we now studied acute energy balance during 14 days following weight implantation. Weight loads ($d = 0.8$ cm, $l = 1.4$ cm; light (LI): plastic core, 2–3% of the initial body mass; heavy (HE): metal core, 10% of the initial body mass; no weight/sham-operation (SO), coated with Elvax Wax, Minimitter Co., USA) were implanted into the lower abdominal cavity of male and female FVB mice (in-house breed, aged 4 months, $n = 27$). 14 days after weight implantation, female mice had not changed or slightly increased their initial biological body mass (BBM), while LI and HE males had a lower BBM (-1–2 g) than SO controls. Body composition (DEXA, Lunar PIXImus, USA) on day 3 showed no changes in fat mass. By day 14 fat mass was reduced in HE males ($P = 0.018$ SO vs. HE, $P = 0.044$ LI vs. HE), but did not differ in females ($P = 0.202$). Cumulative energy intake (kJ/14 days) was decreased in HE males ($P = 0.028$ SO vs. HE) but not different between females ($P = 0.281$). Cumulative energy expenditure (kJ/14 days, $n = 6$, indirect calorimetry) did not differ between any groups. We conclude that compensation in BBM occurs as early as 2 weeks following implantation of artificial weight and we propose that adaptive changes in caloric intake are more relevant for that compensation than changes in energy expenditure.

Intestinal glucose absorption is delayed by hydroxycitrate (HCA). P.Y. WIELINGA[a], R.E. WACHTERS-HAGEDOORN[b], B. BOUTER[a], A. NIEUWENHUIZEN[c], H. VERKADE[b], A.J.W. SCHEURINK[a]. [a]*Department of Neuroendocrinology, University of Groningen, PO Box 14, 9750 AA Haren, The Netherlands;* [b]*Department of Pediatrics, Center for Liver, Digestive and Metabolic Diseases, University Hospital, Groningen, The Netherlands;* [c]*Numico Research, Wageningen, The Netherlands*.

Several studies have shown that hydroxycitric acid (HCA) is a food supplement that reduces food intake in rodents. In this study we focus on a possible inhibitory effect of HCA on glucose absorption, which may indirectly explain the food intake reducing effect. In rats, an intragastric (ig) glucose load was infused for 5 min, 2 h after ig administration of either Regulator HCA (310 mg/kg) or vehicle. Before and after infusion, blood samples were withdrawn using a permanent jugular vein catheter. The glucose response to an ig load of glucose (9 ml, 0.123 g/ml ig) was strongly attenuated in the HCA treated group. In the consecutive experiment, glucose (2 ml, 0.123 g/ml) was given intraduodenally (id). This still resulted in an attenuated blood glucose response, excluding delayed gastric emptying as the underlying mechanism. We used Steele's isotope dilution method to investigate whether a reduced intestinal glucose absorption may explain the attenuated glucose response after ig and id glucose infusion. The data revealed that HCA treatment caused a delay of glucose absorption from the gut into the circulation. The total uptake during the experiment, as reflected by the area under the curve, was not different in the two groups. In conclusion, the data suggest that HCA may delay the removal of glucose from the gut which may contribute to the satiating effect of HCA on food intake.

Influence of motivational state (food-restriction) and food intake on striatal preproenkephalin and hypothalamic neuropeptide Y gene expression profiles. M.J. WILL, V.M. VANDER HEYDEN, T. LAVAUTE, A.E. KELLEY.

The current study explored the influence of motivational state and food intake on striatal preproenkephalin (PPE) and hypothalamic neuropeptide Y (NPY) gene expression. Rats were either food restricted to 80% of their original body weight over a 2-week period (Days 1–14), or allowed access to food (standard chow) ad libitum. Food restricted rats were always fed at 1800 h, 1 h prior to lights off at 1900 h (12:12 h light–dark cycle). On day 15, half of the subjects in each treatment group were given access to food, or no food at 1800 h, and then were sacrificed at 2030 h. Levels of both PPE and NPY gene expression were analyzed by Northern blot and in situ hybridization methods. Results of both methods determined that the motivational state induced by food restriction had no influence on striatal PPE gene expression. However, access to food on the last day resulted in significantly lower levels of striatal PPE expression in both food-restricted and ad libitum fed groups. In contrast, the results of hypothalamic NPY gene expression followed the opposite pattern. Regardless of access to food on the last day, both food restricted groups demonstrated higher levels of hypothalamic NPY gene expression. These results suggest that striatal enkephalins are selectively responsive to food intake, and motivational state induced by food restriction has little or no effect on this process. Such a profile suggests that striatal enkephalin activity may be directly related to hedonic aspects of food ingestion rather than energy balance.

Dissociation of ingestive and thermal responses to lipopolysaccharide in chronic decerebrate rats. D.L. WILLIAMS, L.A. SADACCA, J.S. CARMODY, J.M. KAPLAN, H.J. GRILL. *University of Pennsylvania, Philadelphia, PA, USA*.

Lipopolysaccharide (LPS) derived from gram-negative bacteria is commonly used in rodents to model pyrogenic infection. Peripheral LPS treatment results in fever and anorexia thought to be provoked by cytokine signaling in the brain, with a focus on hypothalamic mediation. However, LPS administration activates neurons in caudal brainstem nuclei relevant to the control of feeding and thermogenesis, including the NTS and VLM, raising the possibility that hindbrain structures contribute to LPS-induced anorexia and fever. Here, we asked whether neural communication between the forebrain and hindbrain is required for hypophagic and thermal responses to LPS. Chronic decerebrate (CD) rats and neurally-intact controls were given intra-peritoneal injections of LPS (100ug/kg) or saline vehicle prior to an intra-oral intake test session (0.3 M sucrose delivered at 1 ml/min). Brown adipose tissue (BAT) temperature was measured from 3 to 8 h after treatment. The anorexic response to LPS was significant in both intact and CD rats, with both groups reducing intra-oral intake by approximately 65%. LPS induced thermal responses in both intact and CD rats. Hyperthermia of nearly 2 °C was apparent in neurally intact rats. By contrast, LPS treatment reduced BAT temperature in CD rats by approximately 2 °C. Our results demonstrate that the isolated caudal brainstem is sufficient for an anorexic response to bacterial infection. Intact connections between the forebrain and hindbrain are required, however, for the expression of the febrile response to LPS observed in intact rats. The absent thermogenic response in CD rats may reflect altered dose-response relationships, a shift in balance between thermogenic and hypothermic effects of LPS, or disrupted function/absence of critical thermogenic triggers within the caudal brainstem.

Programming metabolic systems through early postnatal nutrition in the rodent. S.M. WILLIAMS, X.Q. XIAO, B.E. GRAYSON, M.S. SMITH, K.L. GROVE. *Division of Neuroscience, Oregon National Primate Research Center, OHSU, Beaverton, OR 97006.*

In the past decade, there has been a dramatic increase in obesity and type II diabetes among children. Recent data indicates that 10-15% of children are obese, with twice that number being overweight. Nutrition during critical periods of development is likely a major contributor to this increase. The purpose of this study was to investigate the long-term impact of nutritional manipulations specifically during the postnatal period on the metabolic systems in the skeletal muscle (SkM) and brown adipose tissue (BAT) of the rat. For these studies we raised rats in varying litter sizes that cause abnormal body weight phenotypes as adults: 8 pup litters - controls; 3 pup litters - obese/diabetic; 14 pup litters - lean/diabetic. We utilized real time PCR and Western blot analysis to investigate several genes/proteins that are involved in maintaining metabolic homeostasis at different postnatal ages. Surprisingly, although the animals raised in 3 pup litters were obese as adults, they displayed significantly elevated levels of uncoupling protein 1 (a major regulator of BAT thermogenesis) mRNA and protein, suggesting that these animals were attempting to compensate through increased BAT thermogenesis. In contrast, lean animals had normal UCP1 mRNA but dramatically lower UCP1 protein levels, indicating that they were conserving energy. Both of these groups displayed high-normal Glut4 (the major insulin dependent glucose transporter) mRNA in SkM, but had significantly lower Glut4 protein expression, which is likely a major contributor to the insulin resistance displayed in both of these models. These results support the hypothesis that simple nutritional manipulations during the postnatal period can cause abnormal programming of metabolic systems, predisposing the animals to metabolic disturbances as adults.

Melanocortin agonists alter the defended level of body adiposity. K.A. WILMER, R.J. SEELEY. *Department of Psychiatry, University of Cincinnati, Cincinnati, OH 45237-0506.*

Energy balance is regulated by a complex network of peripheral signals that reflect the amount of adipose tissue and CNS neuropeptides that influence food intake and energy expenditure. One of the key CNS systems are the melanocortins and melanocortin-4 receptor agonists potently suppress food intake and cause weight loss in rodents. Endogenous activity of the melanocortin system is influenced by peripheral adipose signals. These peripheral adipose signals do not influence food intake directly. Rather, they appear to alter the defended level of body adipose mass and food intake is altered secondarily in service of that adipose mass goal. To test the hypothesis that the melanocortin is similarly involved in body adipose regulation, we administered the melanocortin agonist MTII SC via 28 day osmotic minipump (0.3 mg/kg/day) to rats that had either been ad lib fed or had been exposed to 2 weeks of either 30 or 60% food restriction. In the ad lib fed rats, body weight decreased by approximately 10% compared to vehicle treated rats with a concomitant decrease in body fat. Interestingly, both food restricted groups ended the experiment at the same absolute body weight and body fat as the ad lib fed rats while the vehicle treated rats were hyperphagic and gained weight. Thus, regardless of the starting weight, MTII-treated rats ended up at the same lowered body weight and body fat. This outcome indicates that changing the level of melanocortin signaling alters the defended level of body adiposity and that food intake is altered secondarily to achieve this level of defended level of body adiposity. This work was supported by grants from NIDDK and funds from the Procter & Gamble Co.

The Effects of Aminopeptidase Inhibitors on Central AngII and AngIII induced Thirst and Salt Appetite. W.L. WILSON, J.W. HARDING, J.W. WRIGHT. *Department of Psychology, Department of VCAPP, Washington State University, Pullman, WA 99164, USA.*

The current study examined the effects of thirst and sodium appetite in response to intracerebroventricular (icv) infusions of the two metabolically resistant analogs, [D-Asp©öD-Arg© ÷]AngII and [D-Arg©ö]AngIII (125 or 1250 pmol), and were preserved from degradation by pretreatment with the aminopeptidase A inhibitor EC33 or the aminopeptidase N inhibitor PC18 (20 μg/min). Prior to icv infusions, rats were sodium depleted with furosemide (10 mg/kg) followed by the angiotensin converting enzyme inhibitor captopril (100 mg/kg) in order to block endogenous angiotensin formation. Both [D-Asp1D-Arg© ÷]AngII and [D-Arg-©ö]AngIII were capable of producing fluid intakes of water and 0.3 M NaCl solution following furosemide and captopril treatment. Icv [D-Arg©ö]AngIII increased water intakes in response to the highest dose but did not effect saline intakes. The higher dose of [D-Asp©öD-Arg© ÷]AngII failed to increase either water or saline intakes. Pretreatment of both EC33 and PC18 decreased water and saline intakes in response to [D-Asp©öD-Arg© ÷]AngII, whereas pretreatment of PC18 extended the duration of [D-Arg©ö]AngIII-induced water and saline intakes. The ability of both inhibitors to block the AngII analog-induced intakes in combination with the prolonged response of the AngIII analog due to preventing its metabolic degradation, strongly suggest that AngIII is the active ligand in centrally mediated thirst and sodium appetite.

Changes in Food Intake and Body Mass Index of Children over a Ten-Year Period. J.F. WILSON, M. MEHICIC, T. BEAVERSON, D.Y. CARTER S. FAHRBAUGH. *Wittenberg University, Springfield, OH.*

In a study of 135 children, aged 18–60 months, who were served lunch twice a week for 12 weeks, Wilson (2000) found that the children drank large quantities of chocolate milk without decreasing their intake of other food items available at the meal, demonstrating that preschool children are unable to regulate energy intake when served high-energy beverages at a meal. The purpose of this experiment was to examine energy intake regulation in the same children, ten years later. The participants were 14 of the original 135 children, now aged 11–15 years. Of the original 135, 58 children were located, and 14 (7 girls and 7 boys) agreed to participate. One menu (consisting of macaroni and cheese, green beans, buttered whole wheat bread, and applesauce) was served twice over 2 weeks, once with sucrose-sweetened chocolate milk and once with aspartame-sweetened chocolate milk in a counterbalanced order. Intakes of all food items and beverage were measured, and Body Mass Index (BMI) for each child was calculated. Subjects consumed significantly more energy from the sucrose-sweetened than from aspartame-sweetened chocolate milk. They also consumed significantly more food at the meal served with sucrose-sweetened milk compared to the meal served with aspartame-sweetened milk. Like preschool children, older children do not show caloric compensation at meals when served a high-energy beverage. No significant correlation was detected between the participant's preschool BMI and the BMI measured 10 years later. Preschool BMI was not significantly associated with any food intake variables measured 10 years later. Present BMI was significantly and positively correlated with the amount of chocolate milk consumed as a preschooler, but no other preschool food intake measures were associated with present BMI or present food intake measures.

The role of attention in overeating. G.L. WITCOMB, J.M. BRUNSTROM. *Department of Human Sciences, Loughborough University, Loughborough LE11 3TU, UK.*

Dietary restraint is associated with paradoxical bouts of overeating. This 'disinhibition' is thought to occur following a lapse in attention to dietary control. In experiment 1, we inferred the extent to which attention is directed to food during a meal by measuring performance on a concurrent cognitive task. Using this novel methodology, we found that larger meal sizes are indeed associated with decreased attention to food. In a similar experiment (experiment 2), some individuals reported actively 'using' the concurrent task to avoid cognisance of their eating behaviour. Consistent with their claim, these 'task users' outperformed 'non-task users' and consumed more food (albeit only in non-dieters), suggesting that they engaged in 'proactive disinhibition'. In experiment 3, we sought to explore this phenomenon in a context that has greater ecological validity. Participants were allowed access to a palatable snack for 5 min. During this period, they were also offered the opportunity to complete a word-search task. Consistent with the hypothesis that attention influences eating, those individuals who chose to complete the word search also consumed significantly more food. In this case, however, we found little evidence that this group engaged in proactive disinhibition. Thus, it would seem that dietary control might also be governed by a more general failure to allocate sufficient cognitive resource during a meal. By this account, a concurrent task may draw attention away from the visceral sensations that develop during a meal. Consistent with this idea, in experiment 4, we found that ratings of desire-to-eat attenuate throughout a meal. However, participation in a concurrent distractor task retards this process. Taken together, these preliminary results indicate that attention has a subtle yet cogent effect on human dietary control.

Flavour–flavour learning is influenced by restrained eating and attitudes towards food. G.L. WITCOMB, J.M. BRUNSTROM. *Department of Human Sciences, Loughborough University, Loughborough, LE11 3TU, UK.*

When a novel flavour (CS) is paired repeatedly with a liked or disliked flavour (US), the CS can acquire the valance of the US. Previously, we have found that this 'flavour–flavour learning' may not be evident in restrained eaters. This is important, because it might explain why learning is more robust in animals than in humans. In the present set of experiments, we explored reasons why learning might be modulated by restraint status (restrained/unrestrained). In experiment 1, flavour-flavour learning was compared across three groups; dieters, restrained eaters, and unrestrained eaters. Contrary to our earlier work, we found that while the unrestrained eaters acquired a positive evaluative response, our restrained eaters developed a dislike for the CS. Dieters showed little valance shift in either direction. One explanation is that the valance of the US (negative or positive) is governed by associated beliefs and attitudes. In experiment 2, we manipulated beliefs about a novel candy US by labelling it as either 'high calorie' or 'low calorie'. Our results confirmed that restrained and unrestrained eaters acquire a negative and a positive evaluative response, respectively. However, this was only the case when the US was labelled 'high calorie.' This suggests that the quality and efficacy of the US may be governed by beliefs about the threat that it poses to dietary control. Moreover, contrary to previous accounts, it implies that flavour–flavour associations should not be characterised as a simple form of associative learning.

Oral ingestion of 10% ethanol does not increase CCK-induced c-Fos expression in the Nucleus Tractus Solitarius (NTS) of Sardinian alcohol-preferring (sP) rats. A. WOLFE[a], M. MASSI[b], N. GEARY[a]. [a]*Bourne Laboratory, NY Presbyterian Hospital-Weill Cornell Medical College, White Plains, NY 10605, USA;* [b]*Department of Pharmacological Sciences and Experimental Medicine, University of Camerino, 62032 Camerino, Italy*.

We have previously reported that (1) that intragastric gavage of 10 ml 10% ethanol increased c-Fos expression in the NTS of male sP rats, (Soc Neurosci Abstr, 2003) and (2) intraperitoneal (IP) injection of CCK-8 decreases sP rats' 10% ethanol intake under similar conditions (Appetite 2002; 39, 107). Here we attempted to link these findings by testing the joint effect of voluntary intake of 10% ethanol and IP CCK-8 on NTS c-Fos expression. Twenty nine male sP rats that otherwise had ad libitum access to 10% ethanol, food, and water were deprived of ethanol, but not of food or water, for 22 h once every 3rd or 4th day. On the test day, rats were offered 10% ethanol or not at the end of the deprivation period. Rats that ingested 3 ml ethanol within 15 min and rats that were not offered ethanol were then IP injected with 4 μg/kg CCK-8 or with saline alone. Rats were anesthetized and perfused 90 min later, and 40 μm coronal brain sections subsequently processed for c-Fos immunocytochemistry. CCK increased c-Fos expression markedly in the NTS just caudal to the AP, in the subpostremal NTS, and in the NTS just rostral to the AP. Ethanol ingestion, however, had no effect on NTS c-Fos expression in either saline-injected or CCK-8-injected rats. These data fail to reveal any interactive effect of voluntary ethanol ingestion and CCK-induced negative feedback on processing of gut-related feedback information in the NTS. Support: AA 12880.

The role of thermogenesis in the resistance to diet induced obesity. C. WULLER, M.J. MORRIS, B.J. OLDFIELD. *Howard Florey Institute, University of Melbourne, 3052 Austrlalia*.

It is well established that Sprague Dawley rats when exposed to a high fat diet exhibit a bimodal weight gain similar to that seen in human populations. There is a pervasive view that the different weight gain seen in obese prone (OP) and obese resistant (OR) rats reflects a genetically-determined difference in energy expenditure. In these experiments, rats were fed a high fat cafeteria diet and both thermogenic activity in BAT and physical activity were measured using telemetry. During the 15 weeks of the diet, OP rats consumed 23% more energy than OR rats but gained 93% more weight. Similarly, OR rats consumed 76% more energy than controls (fed chow) but gained 7% less weight. These discrepencies may be explained by the fact that the average BAT temperature was higher in the OR than the OP rats ($P < 0.001$). Resting energy expenditure was greater in the OR group for most of the feeding regime but there was no difference in physical activity. Circulating levels of leptin were higher in the OP group which reflected levels of body fat. These data show that thermogenesis in BAT is elevated in OR rats and this may at least partly explain the ability of these animals to defend their body weight in the face of a high fat diet.

Exercise decreases the CCK response to a meal. E.C. WUORINEN[#], C. BURANT, K.T. BORER. *Movement Science, Division of Kinesiology and Internal Medicine, The University of Michigan, Ann Arbor, MI.*

Cholecystokinin (CCK) is a hormone that induces satiety following a meal (Degan et al., 2001; Kissileff, et al., 1994). CCK was also reported to be secreted in response to vigorous exercise (Bailey, et al., 2001; Sliwowski, et al., 2001). It is not known whether the energy deficit caused by exercise affects the secretory pattern or the satiating effect of CCK. Therefore, we hypothesized that exercise in a fasted or post-absorptive state will suppress the release of CCK and sensation of fullness in response to a meal. Eight postmenopausal women engaged in moderate intensity exercise in the form of an AM and a PM 2-h bout of walking, expending approximately 400 kcal above the resting metabolic rate. Exercise was timed either before (ExBM) or after (ExAM) each of two daily isocaloric meals. We evaluated the effects of exercise and meals on plasma CCK concentrations and ratings of fullness via visual analog scale. Energy expenditure was measured by indirect calorimetry. Doubling the caloric expenditure of exercise during the ExBM condition (800 vs. 400 kcal) led to a smaller postprandial secretion of CCK, (AUC 345.76 vs. 246.90 pmol/l, $P = 0.025$). CCK response in both trials was greater to the first meal (eaten after 400 kcal expenditure) than to the second meal (eaten after 800 kcal expenditure, AUC 682.97 vs. 535.52 pmol/l, $P = 0.02$). In contrast, the postprandial rating of fullness was unaffected by exercise or the magnitude of associated energy expenditure. Our results suggest that energy expenditure of exercise diminishes the satiating effect of a meal and thereby produces a physiological compensatory mechanism for restoration of energy balance in the absence of psychophysical detection of this compensation.

Molecular mechanisms of peripheral metabolic adaptations during lactation. X.Q. XIAO, K.L. GROVE, M.S. SMITH. *Division of Neuroscience, Oregon National Primate Research Center, Beaverton, OR 97006*.

Lactation and fasting are physiological conditions characterized by negative energy balance. Following parturition, various alterations occur in the dams that allow her to adapt to the energy demand of milk production. Brown adipose tissue (BAT) and skeletal muscle (SkM) are key sites to control energy expenditure and metabolism of fuel substrates. Real-time PCR and Western immunoblot analysis demonstrated that, compared with diestrous rats, UCP1 and UCP3 in BAT was dramatically reduced at day 11 of lactation and after 48 h of food deprivation, indicating a similar significant decrease in energy expenditure under these conditions. Exogenous leptin or removal of pups for 48 h completely reversed the downregulation of UCP1 and UCP3 mRNA expression in BAT. These results highlight the significance of lower leptin level in mediating energy expenditure during lactation and fasting. In contrast to BAT, UCP3 expression in SkM was differentially regulated; fasting significantly increased, while lactation decreased, mRNA and protein expression of UCP3, suggesting the utilization of fatty acid as a fuel source is spared during lactation. As in BAT, leptin treatment and removal of pups were able to restore changes in UCP3 mRNA expression in SkM during lactation. Further analysis using cDNA microarrays identified several important gene products that may function as upstream modulators of UCP3 expression. In addition, a coordinated upregulation of gene transcripts for key enzymes in glycolysis, and down-regulation of genes in the TCA cycle during lactation were observed. These results suggest differentially regulated UCP3 expression and metabolism of fuel substrates during lactation and fasting suggested that lactating rats actively spare fatty acid for the milk of production, but conserve energy through reduced BAT thermogenesis.

The role of the hypothalamic neuropeptides on ingestive behavior of taste fluid in rats. T. YAMAMOTO, Y. FURUDONO, C. ANDO. *Department of Behavioral Physiology, Graduate School of Human Sciences, Osaka University, 1-2 Yamadaoka, Suita, Osaka 565-0871, Japan*.

Recent studies show that various hypothalamic neuropeptides are involved in the regulation of energy homeostasis and food intake regulation. Although orexigenic neuropeptide injections induce food intake, the relationship between neuropeptides and taste preference is unclear. Our previous study determined the effects of intracerebroventricular (i.c.v.) hypothalamic neuropeptides injections on distilled water and 5 mM saccharin fluid intake. The peptides used were ghrelin, agouti-related protein (AgRP), dynorphin-A (DYN), orexin-A (OXA), melanin-concentrating hormone (MCH) and neuropeptide Y (NPY). Although ghrelin, AgRP and DYN showed no effects on the intake of both water and saccharin, MCH and OXA significantly increased the intake of both fluids. NPY significantly increased saccharin, but had no effect on consumption of water intake. The purpose of the present studies was to investigate the mechanism behind the intake increase observed and the correlation between neuropeptides and taste preference. First, we examined the effect of taste solution intake on hypothalamic peptide mRNA expression. Although water and saccharin intake had no effect on MCH mRNA expression levels, saccharin intake, but not water intake, stimulated orexin-A and NPY mRNA levels. Sweetness-induced hyperphagia altered mRNA levels of both peptides in the hypothalamus. Second, we examined whether MCH, orexin-A or NPY elicits fluid intake via opioid receptor activation. A dose of naloxone (0.3 mg/kg, ip) that had no effect on its own reduced the acute orexigenic effect of icv orexin-A and NPY. However, this same dose of naloxone had no effect on icv MCH-induced hyperphagia. The results of the present study suggest that orexin-A and NPY regulate ingestive behavior based on taste preference

Effects of taste perception on digestion, stress and immunity in rats. C. YAMAMOTO, T. YAMAMOTO. *Department of Behavioral Physiology, Graduate School of Human Sciences, Osaka University, Osaka, Japan*.

It is known that taste and smell play a role in appetite, food choices and nutrient intake. To further examine the role of taste in this respect, the following three experiments were performed in Wistar male rats. First, we examined the effect of taste of food on its digestion in the stomach. Rats were randomly divided into four groups: each group was trained to eat a mash (8 g) made up with powdered food and a liquid. The liquid was either distilled water, 0.1 M Na-saccharin, 0.25 M sucrose or 0.01 M quinine hydrochloride. On the test day, the content of the stomach of each rat was measured 150 min after the start of eating the mash. It was shown that the food output from the stomach was increased by the sweet and palatable food in comparison with non-adulterated food, whereas it was decreased by the bitter and aversive food. In the second experiment, we measured the level of serum corticosteron (CORT) to examine the role of taste perception as a stresser. The level of CORT was increased by ingestion of a mash with the taste of quinine. In the third experiment, we measured the level of serum interleukin-1b (IL-1b) and interleukin-2 (IL-2) in the serum to examine the effect of taste perception on the immunity. The level of IL-2 was increased by the sweet mash in comparison with the non-adulterated food, and the level of IL-1b was decreased by the bitter mash. These results show that palatable tastes increase the digestive function and immunity, whereas aversive tastes decrease the digestive function and induce stress, suggesting that palatable foods are good for health.

Role of noradrenergic transmission in the amygdala in retrieval of long-term taste aversive memory. Y. YASOSHIMA[a], T. YAMAMOTO[b], K. KOBAYASHI[a]. [a]*Dept Mol Genet, Inst of Biomed Sci, Fukushima Med Univ., 960-1295 Japan;* [b]*Dept Behav Physiol, Graduate School of Human Sci, Osaka Univ., 565-0871 Japan.*

Noradrenergic transmission plays an important role in long-term memory formation. Mice heterozygous for the mutation in the gene encoding tyrosine hydroxylase (TH), a rate-limiting enzyme in the biosynthesis of catecholamines, impair long-term memory because of reduced noradrenaline metabolism. Here we report the role of noradrenergic modulation in retrieval process of gustatory memory of conditioned taste aversion (CTA). In the CTA paradigm, the ingestion of a conditioned stimulus (CS, 0.5 M sucrose) was paired with the following an i.p. injection of 0.15 M LiCl (unconditioned stimulus, US). After twice pairings of the CS and US, TH mutant mice showed strong aversion to the CS at the first retention test (T1) carried out 24- or 48-h after the pairing. However, the mutants showed impaired retention at the next test 24-h later (T2). A systemic injection of desipramine (15 mg/kg, i.p.), an uptake inhibitor of noradrenaline, before T2 restored the aversive memory in the mutants. Intra-amygdala infusion of β-adrenergic agonist, isoproterenol, before T2 also improved CTA memory in the mutants. These results suggest that upregulation of noradrenergic transmission in the amygdala facilitates retrieval of long-term memory in conditioned taste learning.

Changes in the sensory and hedonic characteristics of odours conditioned by association with tastants. M.R. YEOMANS, S. MOBINI, T.D. ELLIMAN, H.C. WALKER. *Department of Psychology, University of Sussex, Brighton, BN1 9QG, UK.*

Previous reports indicate that the rated sweetness of novel odours can be modified associations of the odour with a sweet taste (e.g. Stevenson et al., Chem Senses 24 (1999) 627–635). The same studies consistently fail to find equivalent changes in hedonic evaluation of trained odours. However, in this context 'sweetness' ratings might themselves reflect hedonic evaluations. The present experiments were designed to test whether conditioned changes in sensory characteristics operated independently of hedonic changes. In Experiment 1, 24 participants made hedonic, sweet, salty and 'meaty' evaluations of three odours presented orthonasally before and after training. Training trials consisted of the same evaluations being made for retronasal experience of these odours paired with either 10% sucrose, a compound of monosodium glutamate and NaCl (MSG), or water (control). As predicted, the rated sweetness of the odour paired with sucrose increased, while both salty and meaty ratings were preserved for the MSG-paired odour relative to sucrose and control-paired odours. Pleasantness of all three odours decreased, but more so for the MSG-paired odour. However, change in pleasantness of the sucrose-paired odour correlated with the rated pleasantness of sucrose during training ($r = 0.49$, $P < 0.001$). In Experiment 2, participants were pre-selected as sweet likers, and an overtly aversive stimulus (quinine) replaced MSG during training, which was disguised, with no evaluations of retronasal stimuli, to reduce expectancy effects. Both sweetness and pleasantness increased for the sucrose-paired odour, whereas bitterness increased but pleasantness decreased for the odour paired with quinine. Together these data confirm the strength of olfactory conditioning, and suggest that conditioned changes in sensory and hedonic evaluations operate independently.

Deprivation effects on nutrient conditioned flavor acceptance and preference in rats. E. YIIN[#], K. ACKROFF, A. SCLAFANI. *Department of Psychology, Brooklyn College of CUNY, Brooklyn, NY, USA.*

The postingestive actions of nutrients condition strong flavor preferences in rats and may also stimulate increased flavor acceptance (total intakes) in some situations. This study determined the impact of food deprivation on flavor preference and acceptance conditioned by intragastric (IG) infusions of glucose. Rats fitted with gastric catheters were food restricted (FR; 2 h/day) or had food ad libitum (AL). Both groups were trained (20 h/day) to associate a CS + solution (bitter or sour) with IG 16% glucose and a CS − solution with water infusions. During one-bottle training, FR rats consumed substantially more CS + than CS − (49 vs. 8 g/day) whereas AL rats drank only slightly more CS + than CS − (29 vs. 23 g/day). Both groups displayed strong CS + preferences in two-bottle choice tests (90%). When the AL rats were food restricted they drank substantially more CS + than CS − (35 vs. 6 g/day; one-bottle non-reinforced tests) although their CS + acceptance was not as pronounced as that of FR rats. When both groups were given food ad libitum they consumed similar amounts of CS + which were only slightly greater than their CS − intakes in one-bottle tests (25 vs. 20 g/day). Their two-bottle CS + preference remained strong (90%). Thus, food restriction did not enhance flavor preference learning but increased CS + flavor acceptance. The post-training changes in flavor acceptance produced by food restriction indicate that it primarily affected the expression rather than the acquisition of flavor acceptance. Nondeprived animals learn to associate flavors with nutrition and increase their flavor acceptance when in energy need even in the absence of nutrient feedback.

Supported by NIH Grant DK-31135.

Body weight, fat-distribution and accumulation in OLETF and LETO rats: ontogeny and reproductive status. O. ZAGOORY#, M. SCHROEDER, S. BI, T.H. MORAN, A. WELLER. *Department of Psychology, Gonda Brain Res Ctr, Bar-Ilan Univ, Israel, Johns Hopkins Univ Med Sch, USA*.

Adult OLETF rats lacking expression of functional CCK-A receptors are hyperphagic and become obese. We followed-up the patterns of body-weight gain and fat-pad distribution of OLETF and LETO (control) rats, from postnatal day 1 to 65. OLEFT pups were significantly heavier since birth and gained weight more dramatically from the third postnatal week, compared to LETO controls. Accumulation of Brown fat and three White fat-pads: Retroperitoneal, Ingual and Epididymis was investigated. The developmental trajectory of accumulation of Brown fat in OLETF and LETO males did not differ. In contrast, OLETF tended to accumulate Ingual and Retroperitoneal fat pads from post weaning period and on, while accumulating more Epididymal white fat than LETO only in adulthood. We are currently analyzing the mRNA of NPY and POMC in hypothalamic brain sections of these pups; data will be shown. We further investigated white fat-accumulation, Ingual and Retroperitoneal, of OLETF and LETO (25–30 weeks-old) females on weaning day, 8 weeks post-weaning and virgins. These fat pads of LETO females were largest (when normalized to body weight) at weaning compared to the levels found in post-weaning and virgin females. But the fat pads of OLETF females were heavier in virgins and lighter at weaning. Thus, LETO females accumulated fat during pregnancy and lactation, returning to their normal fat levels post-weaning. In contrast, since OLETF rats are hyperphagic, accumulate larger fat pads and become obese, we speculate that the process of fat-accumulation in OLETF females is disturbed by pregnancy and lactating.

Support: US-Israel Binational Science Foundation & Rich Center, Bar-Ilan University.

Role of hypothalamus in nucleus accumbens-induced intake of palatable food. H. ZHENG, H.-R. BERTHOUD. *Neurobiology of Nutrition Laboratory, Pennington Biomedical Research Center, LSU, Baton Rouge, LA, USA.*

The nucleus accumbens (Acb) is thought to be involved in 'liking' of palatable food through its mu-opioid receptors, and in 'wanting' through the mesolimbic dopamine system. Projections to the hypothalamus have been shown to play a key role in increased food intake elicited by inhibiting the medium spiny neurons in the Acb. Based on our earlier findings that appetite-inducing Acb manipulation changes activity of hypothalamic peptidergic neurons (Zheng et al., Am J Physiol, 2003), we hypothesized that these changes may mediate Acb-induced increases in food intake. Specifically, we tested the ability of Y1-receptor blockade to inhibit intake of high fat diet induced by Acb mu-opioid receptor stimulation. Male SD rats, accustomed to high fat pellets but maintained on regular chow, were fitted with cannulas in the Acb and lateral ventricle (LV). In one experiment, ad libitum chow fed rats were injected at 4 h into the light phase with saline or the selective Y1-receptor antagonist 1229U91 (10 μg/3 μl, LV), and high fat pellets made available for 1-h. In another experiment, 1229U91 or saline was injected after the first 1-h bout of high fat intake, followed 15 min later by the selective mu-opioid agonist DAMGO (150 ng/0.3 μl, Acb), and high fat pellets were offered again for 2-h. Y1-receptor antagonism strongly attenuated 1-h contrast-induced high fat intake without Acb-manipulation, and completely blocked subsequent DAMGO-induced high fat intake. These results indicate that activation of hypothalamic NPY neurons and their projections via Y1-receptor signaling play a major role in stimulation of high fat intake induced by Acb-DAMGO and by 'natural' palatability contrast. Supported by NIH DK47348.

Impact of the chemical senses on augmenting memory, attention, reaction time, problem solving, and response variability: The differential role of retronasal versus orthonasal odorant administration. P. ZOLADZ, B. RAUDENBUSH, S. LILLEY. *Wheeling Jesuit University, Department of Psychology, Wheeling, W.V.*

Past research has consistently noted a significant interplay between tastes, odors, and human behavior. In addition, odorants have a differential effect on human behavior, dependent upon route of administration (retronasal vs. orthonasal). The present study examined the differential effects of odorants administered retronasally and orthonasally on cognitive performance. Phase I investigated the effects of retronasal odorants on cognition, while Phase II investigated the effects of orthonasal odorants on cognition. During Phase I, 31 participants completed cognitive tasks on a computer-based program (Impact®) under five 'chewing gum' conditions (no gum, flavorless gum, peppermint gum, cinnamon gum, and cherry gum). During Phase II, 39 participants completed cognitive tasks on a computer-based program (Impact®) under four odorant conditions (no odor, peppermint odor, jasmine odor, and cinnamon odor). Results revealed a task-dependent relationship between odors and the enhancement of cognitive processing. Specifically, cinnamon, administered retronasally or orthonasally, improved participants' scores on tasks related to attentional processes, virtual recognition memory, working memory, and visual-motor response speed. Implications of the present study are most promising in providing a non-pharmacological adjunct to enhancing cognition in the elderly, individuals with test-anxiety, and perhaps even patients with diseases that lead to cognitive decline. This study was funded by a grant from Psi Chi to P. Zoladz.