26th Annual Meeting of the Society for the Study of Ingestive Behavior

Printable Program

July 17-21, 2018
Hyatt Regency Coconut Point
Bonita Springs, Florida

Tuesday, July 17, 2018

12:00 - 3:00 PM	Great Egret
SSIB Board Meeting (By Invitation Only)	

4:45 - 5:00 PM	Calusa ABC
OPENING GREETINGS	

Chair(s): Robert Ritter

5:00 - 6:00 PM	Calusa ABC
MARS LECTURE 1	

Chair(s): Scott Kanoski

5:00 **Obesity: A Chronic Disease Long After It Is Supposedly Cured By Weight Loss**

M ROSENBAUM
Professor, Pediatrics and Medicine at CUMC, Columbia University Medical Center, New York, NY, United States

Obesity affects ~35% of adults and 17% of children and accounts for over 20% of U.S. health care costs. Despite multiple new interventions, the likelihood of sustaining non-surgical weight loss (~15%) hasn't changed in over 30 years. This presentation reviews the physiology of cross-talk between adipocytes, the brain, and systems regulating energy intake (behavioral) and output (metabolic) which act coordinately to oppose reduced weight maintenance. In controlled in-patient studies we examined the effects of dietary weight loss on systems regulating energy balance. We, and others, have found that following weight loss, there are changes in skeletal muscle, autonomic, and neuroendocrine functions coupled with increased hunger, delayed satiation, and changes in food-related neuronal activation which conspire to favor weight regain. The magnitudes of these findings are consistent with the behavioral adaptations that are made by those successful at long-term reduced weight maintenance such as those studied in the National Weight Control Registry. Most of these changes in feeding behavior and thermogenesis are "reversed" upon repletion with the adipocyte-derived hormone leptin which is largely ineffective in promoting weight loss in subjects at usual weight or during dynamic weight loss. In summary, obesity is a chronic biological disease which continues to manifest itself as hyperphagia and hypometabolism long after successful weight loss. Post-weight loss interventions – whether behavioral, pharmacological, biological, or surgical should focus on "correcting" the changes in energy homeostasis that occurred as a result of weight loss. The goal of such therapy is to encourage harmonious crosstalk between the CNS and periphery to prevent, rather than promote, weight regain.

6:00 - 8:00 PM	Belvedere/Belvedere Terrace
Opening Reception	

8:00 - 9:00 PM	Mangroves
Graduate Student Happy Hour	

A relaxed, casual gathering and opportunity to mingle with other graduate students over a cocktail! Mangroves will be the exclusive gathering spot for this event. Cash Bar.

Wednesday, July 18, 2018

8:30 - 10:30 AM	Calusa ABC
Presidential Symposium: Uncovering the Cells and Circuits for Glucose Monitoring in the Hindbrain	

Chair(s): Robert Ritter and Harvey Grill

8:30 **Introduction**
H GRILL
University of Pennsylvania

8:45 **Multiple Mechanisms And Responses To Hindbrain Glucose Sensing**
S RITTER, Q WANG, A-J LI
Washington State University, Integrative Physiology and Neuroscience, Pullman, WA, United States

Glucose, the required substrate for brain energy metabolism, is tightly monitored and controlled. Decades of research have shown that hindbrain catecholamine (CA) neurons are critically involved in this process. They are activated during glucoprivation and elicit life-sustaining glucorestorative responses. Our work has focused on the CA circuitry eliciting these responses. Using a CA-selective, retrogradely transported immunotoxin, anti-dopamine beta hydroxylase (DBH) saporin, we identified two distinct populations of CA neurons in the ventrolateral medulla (VLM) that are essential for key glucoregulatotry responses. Retrograde lesion of CA neurons with projections to the hypothalamus permanently abolished corticosterone secretion and feeding specifically in response to glucose deficit, while leaving the same responses to nonglucoprivic stimuli intact. Retrograde lesion of spinally projecting CA neurons eliminated glucoprivation-induced adrenal medullary c-Fos expression and the hyperglycemic response. Additional information regarding the circuitry of glucoregulatory CA neurons has become available with use of genetic and chemogenetic tools. We found that co-silencing of *Npy* and *Dbh* in the central VLM region blocks glucoprivic feeding and that selective chemogenetic activation of CA neurons in this same region increases food intake, corticosterone secretion and c-Fos expression in orexin neurons. In addition, both glucoprivic and chemogenetic activation of VLM CA neurons suppresses CCK-induced activation of dorsal hindbrain CA neurons and reduction of feeding by CCK. These and other results support the hypothesis that hindbrain CA neurons act widely in the central nervous system to elicit essential coordinated responses to glucose deficit.

9:20 **Hindbrain Astrocyte-Neuron Communications In Counterregulation**
RC ROGERS, GE HERMANN
Pennington Biomedical Research Center, Baton Rouge, LA, United States

Astrocytes are associated with the insulation, and maintenance of the neurons they surround. The advent of calcium imaging of slice preparations show that astrocytes actively control synaptic activity and neuronal excitability, especially in homeostatic hindbrain circuits. Examples include vago-vagal control of the gut, generation of respiratory rhythm, feeding behavior and glucose homeostasis, especially counter-regulation. Hypoglycemia triggers counter-regulation responses (CRR) activating feeding behavior, autonomically-mediated mobilization of carbohydrate stores plus a dramatic increase in gastric motility. These responses converge to elevate circulating glucose levels to counter the hypoglycemic threat. Hindbrain catecholamine (CA) neurons in the nucleus of the solitary tract (NST) and ventromedial medulla (VLM) are critical neuronal elements of the circuit triggering these effects. The chemosensory connection between the detection of low glucose and the activation of these CA-autonomic pathways has not been clear, though astrocyte involvement was suspected nearly 20 years ago. Calcium imaging studies reveal that astrocytes in the NST are sensitive to hypoglycemic conditions. CA neurons in the NST and VLM are also sensitive, but their responsiveness depends on gliotransmission. Parallel *in vivo* studies reveal that CRR-mediated increases in glycemia are dependent on intact astrocytes utilizing purinergic gliotransmission. Astrocyte chemosensation emerges as an important component of autonomic and behavioral homeostasis.

9:55 **The Role Of Glucose-Sensing Inhibitory Neurons In The Nucleus Tractus Solitarius In Metabolic Regulation**
BN SMITH

University of Kentucky, Lexington, KY, United States

A distributed system of glucose-sensing neurons in the brain monitors energy status and also contributes to metabolic regulation. This system includes neurons of the brainstem nucleus tractus solitarius (NTS) that sense glucose concentration changes directly and also monitor neural signals generated in the digestive viscera. In particular, GABAergic inhibitory neurons in the NTS receive primary vagal afferent synaptic information and, in turn, potently regulate preganglionic parasympathetic vagal motor neurons via their synaptic connections with neurons in the dorsal motor nucleus of the vagus nerve (DMV). Most NTS GABA neurons are sensitive to changes in [glucose] in a glucokinase (GCK)-dependent fashion. This talk will discuss evidence supporting the general hypothesis that a brainstem-centered glucose regulatory system contributes to systemic metabolic regulation. To wit, in addition to sensing glucose, inhibitory NTS neurons contribute to whole body glucose regulation via modulation of parasympathetic output to the viscera. Modulating GCK activity in the NTS also regulates blood [glucose]. Interestingly, GCK expression and glucose-sensitivity are reduced in the NTS after several days of continuous hyperglycemia in the streptozotocin (STZ)-treated mouse, and both inhibitory and excitatory synaptic control of DMV motor neurons is also functionally altered after diabetes. Neurons in hindbrain autonomic centers are both affected by and contribute to systemic glucose homeostasis, and activity of these neurons is functionally altered by periods of hyperglycemia. Altered neural function in the NTS may reflect a neurogenic component of diabetic pathology, and modulating specific neural function in the vagal system might address diabetes-related glycemic dysregulation.

10:30 - 11:00 AM	Calusa DE
Coffee Break	

11:00 - 1:00 PM	Calusa ABC
ORAL SESSION 1: Hot Topics	

Chair(s): Harvey Grill and Alexandra DiFeliceantonio

11:00 **Influence Of Social Media And Attitudes Towards The Body And Self On Eating Behaviour**

A.Y. SIM[1], T.J. LIM[2], C.L. ZHAO[2], Z.E. QUEK[2], B.K. CHEON[1,2]

[1]Clinical Nutrition Research Centre (CNRC), Singapore Institute for Clinical Sciences (SICS), Agency for Science, Technology and Research (A*STAR) and National University Health System, Singapore, Singapore, [2]School of Social Sciences, Nanyang Technological University, Singapore, Singapore

Research has established the adverse relationship between social media, negative body image and weight-related health issues. However, there is limited experimental support for the direct influence of social media use on resultant body image concerns and actual eating behaviour. Here, we examine whether naturalistic browsing of Facebook (Study 1; n = 89 and Study 2; n = 79) and Instagram (Study 3; n = 59), and the viewing of Instagram-type content (i.e. healthy food and exercise pictures from actual posts) (Study 4; n = 103) may influence portion selection patterns and food intake and the role of body image and self-esteem in this relationship. Study 1 and 2 revealed that among women, Facebook use (vs. control news website) resulted in lowered snack portion selection (restraint) among those reporting increased body dissatisfaction. Similarly, this effect of body discontentment on suppressed eating behaviour (decreased ad-libitum consumption of potato crisps) was also observed following Instagram use (vs. control Instagram profile on engineering content) in Study 3. Study 4 demonstrated that the type of social media content has varying effects on body dissatisfaction and self–esteem, and consequently eating behaviour. While the suppressive effects of body dissatisfaction on snacking behaviour was more pronounced following the exposure to posters eating healthy food, the stimulating effects of elevated self-esteem on snack intake was more evident after viewing posters exercising. Taken together, our findings suggest that social media use and the social comparisons it promotes may influence eating behaviour among those with vulnerable body image and feelings of self-worth.

11:15 **A Unique Population Of Stress Sensitive Neurons In The Female Bed Nucleus Of The Stria Terminalis**

TL FETTERLY[1-3], EK AWAD[2], Y SILBERMAN[4], DG WINDER[1-3]

[1]Vanderbilt Center for Addiction Research, Nashville, TN, United States, [2]Molecular Physiology & Biophysics, Nashville, TN, United States, [3]Vanderbilt Brain Institute, Nashville, TN, United States, [4]Neural and Behavioral Sciences Penn State College of Medicine, Hershey, PA, United States

Stress contributes to many psychiatric diseases. Sex is an important biological variable in responses to stress. Females have a higher prevalence of affective and eating disorders, which are often comorbid and have an underlying stress component. The molecular mechanisms underlying this difference are not well understood. The BNST, a key nucleus in the regulation of stress, is highly sexually dimorphic. Neurons expressing CRF in the mouse BNST are stress responsive as seen by increases in *cfos* expression following acute restraint stress, and this increase is greater in females. To dissect the molecular profile of these neurons, we used fluorescent *in situ* hybridization assays to further characterize the stress-responsivity of BNST CRF neurons. PKCδ has been proposed to mark a population of "fear-off" neurons in the extended amygdala and is largely expressed in CRF-negative cells. Following restraint stress, there is a large increase in the co-expression of *crh* and *prkcd* in cells in the BNST of females but not males. This population is also highly stress-responsive. To investigate the recruitment of these neurons during stress, we used a Gi-DREADD expressing virus injected into the insula or PBN to look at how inhibition of region specific activity can alter the stress response seen in the BNST. For both the PBN and insula manipulations, administering CNO prior to restraint stress blunted the *cfos* increase in *crh* cells in females, but only the insula manipulation altered the response in males. The upregulation of *prkcd* in *crh* neurons was not altered. This data suggests there is a unique population of neurons in the female BNST that is stress sensitive, and the mechanism for recruitment of these neurons may differ as compared to the *crh* population as a whole.

11:30 **Fingerprinting Metabolic Dysregulation And Adiposity In The Brains Of Overweight And Obese Humans**

MC FARRUGGIA[1,2], MJ VAN KOOTEN[2,3], MV BURKE[1,2], D SCHEINOST[4], RT CONSTABLE[1,4,5], DM SMALL[1,2]

[1]Interdepartmental Neuroscience Program, Yale University , New Haven, CT, United States, [2]Department of Psychiatry, Yale University School of Medicine, New Haven, CT, United States, [3]University of Groningen, Faculty of Medical Sciences, Groningen, Netherlands, [4]Department Radiology and Biomedical Imaging, Yale University School of Medicine, New Haven, CT, United States, [5]Department of Neurosurgery, Yale University School of Medicine, New Haven, CT, United States

Neuroimaging work documents altered brain anatomy, function, and connectivity in individuals with obesity and/or diabetes. Whether adiposity and glucose intolerance contribute uniquely to brain dysfunction is unknown. Here we used Connectome-based Predictive Modeling (CPM), to determine if “brain fingerprints” can be isolated for adiposity and metabolic markers. CPM exploits individual variation in whole-brain functional connectivity to predict a behavior/trait that varies across individuals using a leave-one-out procedure. We used CPM to predict body mass index (BMI), waist circumference (WC), and fasting glucose and insulin in 65 overweight and obese individuals (ages 18-45) who were measured for brain response to milkshake (fMRI). fMRI data were first preprocessed, then we created 268x268 functional connectivity matrices and correlated matrix edges (i.e. functional connections) with adiposity and metabolic measures thresholded at $p< 0.01$. Surviving edges were summed to determine network strength. Correlating network strengths with adiposity and metabolic measures in an n-1 linear model generated predictive scores. A map of predictive nodes with a high degree of connectivity was generated to produce the fingerprint for each variable. Fingerprints could be isolated for WC and insulin but not for BMI or blood glucose. The insulin fingerprint included high-degree nodes in prefrontal, cerebellar, occipital, and temporal regions ($r=0.324$, $p=0.01$), while the waist circumference fingerprint had high-degree nodes in amygdala/hippocampus, cerebellar, and temporal regions ($r=0.268$, $p=0.027$). These findings suggest that adiposity and glucose tolerance contribute differently to altered brain function and that waist circumference is more sensitive than BMI.

11:45 **(Nita Award Winner) The Effect Of Experimentally Induced Food Cravings On Energy Intake And Guilt In Frequent Consumers Of Low-Calorie Sweetened Beverages (Lcs)**

NM MALONEY, P CHRISTIANSEN, JA HARROLD, JCG HALFORD , CA HARDMAN
University of Liverpool, Liverpool, United Kingdom

Consumption of low-calorie sweetened (LCS) beverages has become increasingly popular, although their impact on weight loss/maintenance is equivocal. The present study examined whether LCS beverages may have a protective role by satisfying desire for palatable foods, thus helping prevent craving-induced overeating. Participants (N=172) were frequent consumers of LCS beverages who were randomly allocated to one of four conditions in a 2x2 between-subjects design. Participants were exposed to a palatable food cue which they were prohibited to eat (craving condition), or to a non-food related cue (control condition). They were then provided with a selection of sweet and savoury snacks and invited to eat *ad libitum*; LCS beverages were either available with the snack food (available condition) or unavailable (non-available condition). Visual Analogue Scales provided measures of craving and guilt. Results showed a main effect of craving-condition on *ad libitum* food intake (kcal): intake was higher in the craving condition relative to the control condition. There was a main effect of LCS availability; intake was higher when LCS beverages were not available compared to when they were. However, there was no interaction between craving-condition and LCS availability. Participants in the non-available condition reported higher levels of eating-related guilt relative to the condition where LCS beverages were available. These findings suggest that LCS beverages may not be sufficient to prevent craving-induced increases in food consumption. However, participants ate more food overall and felt more guilty regarding their food intake when LCS beverages were unavailable, thus suggesting that frequent consumers may use LCS beverages as an effective strategy to reduce food intake more generally.

12:00 **Sensitivity To Viscosity And Subsequent Estimates Of Expected Satiety Across Different Senses**

C.R. LUCKETT, R. PELLEGRINO, J.D. JONES, G.E. SHUPE
Department of Food Science, University of Tennessee, Knoxville, TN, United States

In beverages, humans use texture (i.e. viscosity) information to estimate calories and expected satiety. While it is widely accepted that texture is a multisensory property, little research has been published how we use senses other than touch to assess texture. This study was designed to compare and contrast the sensitivity of humans to changes in viscosity and estimated satiety through different sensory modalities. Milk samples of varying viscosities were constructed using iota-carrageenan. Fifty subjects were asked to perform a series of 2-alternative forced choice tests, identifying which sample was thicker. Difference thresholds were determined by having a subject consume the samples, listen to the sample pouring, and observing clear vials of the samples. Using vision, subjects were notably less sensitive to changes in viscosity when compared to hearing or oral tactile. Interestingly, oral tactile sensations and hearing were almost identical in their sensitivity to viscosity changes (0.346 cP and 0.361 cP, respectively). Similar patterns were observed when the participants were asked to estimate how full they would be after consuming 1 serving (236 mL) of samples varying in viscosity. In general, participants would rate samples higher in estimated satiety if the difference in viscosity was greater than the calculated difference threshold for a particular sensory modality. This study highlights the relative importance of vision, audition, and touch to forming our sensory judgements regarding viscosity and subsequent satiety estimations.

12:15 **(Nita Award Winner) Oro-Sensory Exposure Or Ingestion Rate? Effects On Satiation And Associated Endocrine Responses**

MP LASSCHUIJT, M MARS, C DE GRAAF, PAM SMEETS
Division of Human Nutrition, Wageningen University & Research , Wageningen, Netherlands

Mastication reduces food intake through increased oro-sensory exposure (OSE) and decreased ingestion rate (IR), but individual contribution of these factors to satiation and physiological processes are unknown. The objective was to determine the effect of concurrent manipulation of OSE and IR on satiation and endocrine responses (pancreatic polypeptide, insulin and ghrelin). Twenty males (23±3 y, BMI 23±2 kg/m2) participated in a 2x2 randomized cross-over study with additional control session (not eating). Participants ate ad libitum of iso-caloric chocolate custards with fudge pieces (chewing; high OSE) or fudge sauce (no chewing; low OSE), in a slow or fast manner (5 or 15 sec between bites). Blood samples were collected at 2 moments before the meal, after meal anticipation and at 5 moments after meal onset. Preliminary analysis showed that in the high OSE conditions participants ate 66 grams less custard compared to the low OSE conditions ($p=0.03$), independent of the IR ($p=0.35$). Pancreatic polypeptide concentration increased first (5 min after meal onset) in the low OSE, fast IR condition ($p=0.005$) and at 10 minutes the concentration was higher compared to the high OSE, slow IR condition ($p=0.03$). During all treatments insulin concentrations increased 8 min after meal onset, prior to a rise in glucose (all, $p< 0.001$). Ghrelin concentrations remained unchanged over the course of the entire meal ($p=0.82$). In conclusion, OSE affects intake independent of IR, and pancreatic polypeptide and insulin responses occur pre-absorptive. Further data analyses will have to show whether the effect of oro-sensory exposure on food intake can be explained by endocrine responses.

12:30 **(Nita Award Winner) Elimination Of Leptin-Responsive Cells In The Ventromedial Hypothalamus Attenuates The Effects Of 4^{Th} Ventricle Leptin Infusions On Weight Loss**

MS SEAMON, RBS HARRIS
Augusta University, Augusta, GA, United States

Leptin, an adipose derived hormone, binds to long form leptin receptors in the brain and prevents weight gain by reducing food intake and increasing energy expenditure. Leptin receptors known to influence energy balance are expressed in the arcuate nucleus, ventromedial nucleus (VMH), and dorsomedial nucleus (DMH) of the hypothalamus, and in the hindbrain nucleus of the solitary tract (NTS). Leptin injected into the 4th ventricle activates receptors in the adjacent NTS, but also *anatomically distant* hypothalamic receptors. The highest levels of hypothalamic activation indicated by the leptin signaling protein, pSTAT3, were found in the VMH and DMH. We tested the importance of the VMH in the control of energy balance by leptin. Leptin conjugated to saporin (leptin-saporin), a ribosome-inactivating neurotoxin that ablates leptin-responsive cells, or control blank-saporin, was injected bilaterally into the VMH. Rats were fitted with 4th ventricle cannulas after 3 weeks, and 10 days later miniosmotic pumps infusing 0.9 μg leptin/day or PBS were attached. A previous study showed this to be the minimum dose of leptin to produce weight loss. Leptin-saporin rats gained significantly more weight than blank-saporin rats before leptin infusion. During leptin infusion, blank-saporin rats had reduced food intake, lower RER, higher daytime energy expenditure and lost body weight and fat. These effects were attenuated in leptin-saporin injected rats. There was a significant increase of pSTAT3 in rats receiving leptin infusions, but leptin-saporin rats showed an expected reduction of pSTAT3 specific to the VMH. Thus, an integrated response between the hypothalamus and brainstem is utilized during weight loss.

12:45 **Neurotensin Receptor-1 Deficiency Increases Risk For Female Mice To Develop Behaviors Similar To Anorexia Nervosa**

LE SCHROEDER, SV PAULS, HL WOODWORTH, GM LEINNINGER
Michigan State University, East Lansing, MI, United States

Anorexia nervosa (AN) has the highest mortality rate of any psychiatric illness but there are no effective treatments to improve body weight. Determining the genetic risk factors that interact with sex and adolescent stress to promote development of AN is necessary to identify pathways for intervention. Recently loss of function variants in the neurotensin and neurotensin receptor 1 (*NTSR1)* gene pathways were identified in individuals with AN. We therefore hypothesize that lacking NtsR1 is a genetic risk factor that interacts with environmental risk factors to increase vulnerability to develop AN. To explore this, we studied male and female NtsR1 knock-out mice ($NtsR1^{KOKO}$) and mice with intact NtsR1 ($NtsR1^{++}$) exposed to environmental risk factors (e.g. adolescent isolation stress and caloric restriction) thought to promote development of AN-like behaviors . NtsR1 deficiency alone promoted low body weight in male and female mice. Yet, female $NtsR1^{KOKO}$ mice exposed to adolescent stress were exclusively vulnerable to developing aphagia, low body weight and co-morbidities similar to those observed in AN. Our work shows that NtsR1-deficiency is a genetic risk factor that acts in concert with sex and adolescent stress to increase vulnerability to develop aberrant behaviors associated with AN. Our findings of a genetic X sex X stress interaction have face validity for AN and are translationally relevant since loss of function variants in the NtsR1 pathway may contribute to development of this disorder. These data support future studies on the precise role of NtsR1 in regulating behavior and body weight to determine if restoration of NtsR1-action could improve outcomes in AN.

11:00 - 1:00 PM	Calusa FGH
ORAL SESSION 2: GLP-1	

Chair(s): Diana Williams and Ted Hsu

11:00 **Endogenous Glp-1 In Lateral Septum Promotes Satiety And Suppresses Motivation For Food In Mice**

SJ TERRILL[1], MK HOLT[1], S TRAPP[2], DL WILLIAMS[1]

[1]Department of Psychology & Program in Neuroscience, Florida State University, Tallahassee, FL, United States, [2]Department of Neuroscience, Physiology & Pharmacology, University College London, London, United Kingdom

Glucagon-like peptide 1 receptors (GLP-1R) are expressed in the lateral septum (LS) of rats and mice, and we have published that LS GLP-1R stimulation affects feeding and motivation for food in rats. We asked if these effects are also observed in mice. Male C57Bl/6 mice were implanted with unilateral cannulas targeting the LS, and in separate dose-response studies, GLP-1 or the antagonist Exendin 9 (Ex9) was delivered before dark onset, at doses subthreshold for effect when injected icv. Intra-LS GLP-1 significantly suppressed chow intake in the first 4 h of the dark phase (up to 82%). However, blockade of LS GLP-1Rs with Ex9 had no effect. We then asked if LS Ex9 blunts nutrient preload-induced intake suppression. Mice were trained to consume Ensure immediately before dark onset, which strongly suppressed subsequent chow intake. Intra-LS Ex9 significantly increased chow intake relative to vehicle under these conditions. We also found that LS GLP-1R blockade attenuated 30-min restraint stress-induced hypophagia in mice. We reported that in the rat, GLP-1R in the dorsal subregion of the LS (dLS) affect motivation for food. We examined this in mice via bilateral delivery of vehicle, GLP-1 or Ex9 to the dLS before operant sessions in which mice earned sucrose pellets on a progressive ratio schedule. In chronically food restricted mice, bilateral intra-dLS GLP-1 significantly suppressed breakpoint (by 58%) and conversely, Ex9 significantly increased breakpoint (20%). The Ex9 effect was still evident after mice returned to ad lib conditions. Together, these data suggest that endogenous activation of LS GLP-1R plays a physiologic role in feeding under some but not all circumstances, and that LS GLP-R activity strongly influences motivation for food.

11:15 **Serotonergic Modulation Of Central Glucagon-Like Peptide-1 Neurons Regulates Energy Balance And Malaise**

RM LEON[1], DJ REINER[1], LM STEIN[1], BC DE JONGHE[2], MR HAYES[1]

[1]Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States, [2]Biobehavioral Health Sciences, School of Nursing, Philadelphia, PA, United States

Glucagon-like peptide-1 (GLP-1) is known for its role in regulating energy balance, stress and motivated behaviors. GLP-1 receptor (GLP-1R) agonists are FDA-approved for obesity and type II diabetes treatment. While the field has gained an understanding of the downstream nuclei targeted by the central GLP-1 system, little is known about the common upstream neurobiological substrates functioning as endogenous activators of this system. Recent literature implicates the serotonergic system as a potential candidate. We hypothesized that serotonin (5-HT) acts as an endogenous modulator of the central GLP-1 system to partition anorectic vs noxious feeding effects of the central GLP-1 system. 5-HT (40μg, 4th ICV) administration reduced chow intake and body weight and increased kaolin intake in rats. Pretreatment with the GLP-1R antagonist, exendin-(9-39) (LV ICV) attenuated the 5-HT-induced anorectic effects at 3 and 24 hours and caused a complete reversal at 1 and 6 hours. Similarly, 4th ICV administration of the agonists for either the 5-HT2C receptor (Lorcaserin, 20μg) or 5-HT3 receptor (SR57227, 20μg) independently suppressed food intake; effects that were also reversed by exendin-(9-39). Lorcaserin acutely suppressed food intake (1 and 3 hr) with no effects on body weight or kaolin intake, whereas SR57227 suppressed food intake at 6 and 24 hours, reduced body weight, and transiently increased kaolin intake. Collectively, these findings suggest a temporal and behavioral (anorectic vs. noxious mediated hypophagia) dissociation between the intake suppressive effects induced by different 5-HT receptor populations. Current experiments are determining if the 5-HTR effect on kaolin intake is dependent on the GLP-1 system. NIH-DK112812.

11:30 **Selective Effects Of Glp-1 Analogues On Hippocampal-Dependent, Learned Inhibition Of Appetitive Behavior In Male And Female Rats**

S JONES[1], C.H. SAMPLE[2], T.L. DAVIDSON[1]

[1]American University Center for Behavioral Neuroscience, Washington, DC, United States, [2]University of Southern California Leonard Davis School of Gerontology, Los Angeles, CA, United States

Glucagon-like peptide-1 (GLP-1) agonists (e.g., liraglutide) decrease meal size and body fat accumulation. It has been proposed that GLP-1 decreases intake by attenuating the value of food reward. Other evidence suggests that GLP-1 agonists may also enhance a hippocampal-dependent process of behavioral inhibition. To distinguish the effects of GLP-1 on reward value from its effects on inhibition, we tested the effects of liraglutide on the ability rats to solve hippocampal-dependent serial feature negative (sFN) discriminations. In Study 1, an excitatory stimulus signaled the delivery of

sucrose, except when it was preceded by the presentation of a negative feature cue. Results indicated that 12 daily ip injections of liraglutide (10 ug/kg,Bachem) increased the power of the negative feature cue to inhibit responding without reducing responding evoked by the excitatory cue. This effect did not vary as a function of sex or maintenance diet (chow vs Western diet (WD)). Liraglutide also reduced body fat gain relative to saline. Study 2 examined the effects of liraglutide (10 ug/kg, i.p. Novo Nordisk) on rats that were trained concurrently on a sFN and on a hippocampal-independent simple discrimination. Only WD-fed male rats exhibited reduced body fat gain following 14 daily injections of liraglutide. Interestingly, only these rats showed enhanced inhibitory responding to the negative feature cue on the sFN task relative to saline controls. Liraglutide did not alter responding to the excitatory cue in the sFN problem and had no effect on the simple discrimination for either sex or diet condition. Both studies suggest that, at doses that reduce body fat gain, liraglutide enhances a hippocampal-dependent form of learned inhibition without diminishing the value of food reward.

11:45 **Preproglucagon Neurons Are The Source Of Brain Glp-1 And Affect Food Intake Under Stress Or After Large Meals**

MK HOLT[1], JE RICHARDS[1], DR COOK[1], DI BRIERLEY[1], F REIMANN[2], FM GRIBBLE[2], S TRAPP[1]

[1]Centre for Cardiovascular and Metabolic Neuroscience, Department of Neuroscience, Physiology and Pharmacology, UCL, London, United Kingdom, [2]Metabolic Research Laboratories University of Cambridge, Cambridge, United Kingdom

Glucagon-like peptide-1 (GLP-1) injected into the brain suppresses food intake. Similarly, chemogenetic activation of preproglucagon (PPG) neurons suppresses feeding. However, the physiological relevance of these effects remains unclear. Here we investigated under which conditions PPG neurons mediate suppression of feeding. First, we proved that PPG neurons are the main source of GLP-1 within the brain. Selective ablation of NTS PPG neurons by viral expression of diphtheria toxin subunit A (DTA) substantially reduced active GLP-1 concentrations in brainstem, hypothalamus, and spinal cord. Interestingly, these mice exhibited no difference in body weight to their littermates injected with control virus. In contrast, short term food intake was affected; DTA-ablated mice ate more chow over a two hour test period following an overnight fast, and substantially more chow after a 15 min Ensure liquid diet preload as compared to control littermates. Using chemogenetic inhibition, we further explored the importance of PPG neuron activity in the control of food intake. We assessed the role of PPG neurons during ad libitum intake, after overnight food deprivation, and following restraint stress. hM4Di-expressing PPG neurons were inhibited in vivo with intraperitoneal injection of 2mg/kg CNO. Acute inhibition of PPG neuron activity did not affect normal feeding, but increased intake after food deprivation and abolished stress-induced suppression of food intake. Our results indicate a role for PPG neurons in hypophagic responses to both large meals and psychogenic stress. These findings suggest that PPG neurons do not simply reduce intake to meet metabolic needs, but are involved in more complex decisions about whether food intake is appropriate in a given physiological context.

12:00 **The Supramammillary Nucleus: A Novel Critical Site Of Glp-1 Control Of Anxiety-Like Behavior.**

L LóPEZ-FERRERAS[1], OT SHEVCHOUK[1], KK EEROLA[1], JE RICHARD[1], FH NILSSON[1], LE JANSSON[1], MR HAYES[2], KP SKIBICKA[1,3]

[1]Institute for Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden, [2]Department of Psychiatry, University of Pennsylvania, Philadelphia, PA, United States, [3]Wallenberg Centre for molecular and translational medicine, University of Gothenburg, Gothenburg, Sweden

Recent studies implicate the gut/brain peptide glucagon-like peptide-1 (GLP-1) in regulation of emotionality, including anxiety behavior; however, the neuroanatomical substrates, from which GLP-1 exerts its anxiogenic effect, remain poorly characterized. Here we examine a relatively uninvestigated candidate nucleus, the supramammillary nucleus (SuM), a nucleus located just caudal to the lateral hypothalamus, and ventral to the ventral tegmental area. Our focus on the SuM is driven by its dense neuroanatomical connections with nearly all brain regions key to anxiety behavior regulation, including the amygdala, dorsal raphe and hippocampus, as well as previous data showing this nucleus is a GLP-1 binding site. We first confirm the potential of SuM to regulate anxiety-like behavior, by showing that chemogenetic (neuronal DREADD/CNO based) activation of neurons in this nucleus results in an anxiolytic response in rats. A GLP-1R agonist, exendin-4, microinjection into the SuM resulted in potent anxiety-like behavior, measured in the open field and elevated plus maze tests in male and female rats, with females displaying a more consistent response. This anxiogenic effect persisted after high-fat diet exposure. This effect was also not altered by any stage of the female estrous cycle. Importantly, reduction of GLP-1R expression in SuM, by AAV-shRNA GLP-1R knockdown, resulted in a clear anxiolytic response; however, only female rats displayed reduced anxiety-like behavior. Our data identify a new neural substrate for GLP-1 control of anxiety-like behavior and indicate the SuM GLP-1R to be sufficient for anxiogenesis in both sexes, but necessary only in females.

12:15 **Glucagon-Like Peptide-1 Receptor Activation In The Lateral Dorsal Tegmental Nucleus Attenuates Cocaine Seeking In Rats**

NS HERNANDEZ, VR WEIR, HD SCHMIDT
University of Pennsylvania, Philadelphia, PA, United States

Glucagon-like peptide-1 (GLP-1) is an incretin hormone and neuropeptide that is produced centrally in the nucleus tractus solitarius (NTS). Emerging literature shows that GLP-1 receptor (GLP-1R) agonists reduce cocaine-mediated behaviors in rodents. The lateral dorsal tegmental nucleus (LDTg) is

a brain region that plays a critical role in cocaine seeking, expresses GLP-1Rs, and receives direct projections from the NTS. Therefore, the present study tested the hypothesis that GLP-1R activation in LDTg plays a critical role in the reinstatement of cocaine-seeking behavior, an animal model of relapse. Using the self-administration/extinction/reinstatement paradigm, rats were pretreated with intra-LDTg infusions of the GLP-1R agonist exendin-4 (Ex-4; 0, 0.005 and 0.025 μg) prior to cocaine priming-induced reinstatement test sessions. We show that intra-LDTg Ex-4 attenuated cocaine reinstatement at a dose that does not affect sucrose seeking or food intake in cocaine-experienced animals. Next, we examined the role of NTS to LDTg projections in cocaine reinstatement using a chemogenetic approach. A cre-dependent neural activating DREADD (hM3Dq) and a cre-expressing retrograde canine adenovirus was infused in the NTS and LDTg, respectively. During reinstatement test sessions, rats were pretreated with clozapine-N-oxide (CNO; 0, 0.1, 1 mg/kg) to specifically activate endogenous NTS to LDTg projections prior to a priming injection of cocaine. We found that selectively activating the NTS to LDTg circuit significantly attenuated cocaine reinstatement. Overall, these results highlight a novel role for hindbrain circuits and GLP-1R signaling in cocaine-seeking behavior.

12:30 **Glucagon-Like Peptide-1 Receptor Agonist, Exendin-4, Reduces Heroin Seeking During Extinction And Drug-Induced Reinstatement**

JE DOUTON, SM BALLARD, PS GRIGSON
Department of Neural and Behavioral Sciences, Penn State College of Medicine, Hershey, PA, United States

Drug addiction has been described as the pathological usurpation of neural systems associated with reward-related learning that directs focus toward drug seeking and drug taking over other rewards. For example, in our rat model of drug-induced devaluation of a saccharin cue, the taste cue precedes access to drug and comes to serve as a predictor of drug availability. As such, it elicits the onset of a conditioned aversive state involving craving and/or withdrawal that is only corrected by drug taking. This phenomenon resembles seeking food when hungry, water when thirsty, or salt when sodium deficient. When these biological drives are activated, there is a single goal and there can be no substitute. In this context, there appears to be a usurpation of the 'need' system rather than the 'reward' system. Recent evidence has shown that hormones involved in hunger and satiety such as glucagon-like peptide-1 (GLP-1) also modulate rewarding and aversive properties of drugs of abuse. Here, we tested for the first time the effects of exendin-4 (Ex-4), a natural agonist of the GLP-1 receptor, on heroin addiction in our model of drug-induced reward devaluation. We observed that treatment with a 2.4 μg/kg dose of Ex-4 did not affect ingestion of the saline- or heroin-paired taste cue. However, we found that in rats that exhibited the greatest heroin-induced devaluation of the saccharin cue, chronic treatment with Ex-4 decreased heroin-seeking during the first hour of extinction. Further, acute treatment abolished drug-induced reinstatement of heroin-seeking behavior in all rats. Taken together, these data support the argument that opioids hi-jack not only reward substrates, but also those mediating the satisfaction of biological 'needs', offering a novel avenue for intervention.

12:45 **Influence Of Glucagon-Like Peptide-1 Analogue, Exenatide, On Anticipatory Food And Alcohol Reward-Hedonic Responses In Human Obesity, And Abstinent Nicotine And Alcohol Dependence**

YY LING[1], LJ NESTOR[1], JN PANNEKOEK [1], F VANELLI[1], S AKAVARAPU [1], K HERLINGHER[1], F AIANO[1], B KOBSON[1], MR MUNAFO[2], AR LINGFORD-HUGHES[1], DJ NUTT[1], AP GOLDSTONE[1]

[1]PsychoNeuroEndocrinology Research Group, Neuropsychopharmacology Unit, Centre for Psychiatry, Division of Brain Sciences, Imperial College London, Hammersmith Hospital, London, United Kingdom, [2]MRC Integrative Epidemiology Unit, School of Experimental Psychology, University of Bristol, Bristol, United Kingdom

Obesity and alcohol dependence are associated with altered reward-stress responsivity. The satiety gut hormone glucagon-like peptide-1 (GLP-1) and its analogues supress consumption and reward responses to food and alcohol in animals, and to food in humans. Our MRC-funded Gut Hormones in Addiction study is investigating if acute intravenous infusion of the GLP-1 analogue, Exenatide (or desacyl-ghrelin) attenuates behavioural components of addiction and overeating in: (i) dieting obese, or abstinent (ii) nicotine- or (iii) alcohol-dependent adults. Outcome measures include reward system activation during a fMRI picture evaluation task for high-energy food and alcohol cue reactivity, craving ratings, and approach bias using an approach-avoidance task. In obese subjects (n=16), Exenatide (vs. Saline) reduced appeal of and activation in nucleus accumbens (NAcc) to alcohol, but not food, pictures. In ex-smokers (n=14), Exenatide reduced activation in NAcc, caudate, putamen, amygdala and insula to food, but not alcohol, pictures. In ex-alcohol dependent subjects (n=10), Exenatide reduced the appeal of food and alcohol pictures, and activation in caudate, putamen and amygdala to alcohol pictures. Exenatide reduced alcohol craving (Alcohol Urge Questionnaire) in each group. In those with higher approach bias at Saline visit, Exenatide reduced approach bias to both food and alcohol in the obese and ex-alcohol dependent group, and to food in ex-smokers. These initial results provide the first evidence in humans that activation of the GLP-1 system can reduce reward-hedonic responses to alcohol, as well as food, including in clinically relevant populations. This provides preliminary proof-of-concept for the potential of GLP-1 analogues to prevent relapse during alcohol abstinence.

1:00 - 3:30 PM	Calusa Foyer
Lunch on Own	

Salads, Sandwiches, Hamburgers and Hot Dogs will be available for purchase by CASH or hotel room charge in the Calusa Foyer. Price Range ($10-$15)

1:00 - 2:30 PM	Calusa ABC
Professional Development: Grant Writing	

After attending this workshop, young investigators and early career researchers will have a better understanding of the NIH grant application process, and will appreciate the different roles played by NIH institutes, programs and review groups and their personnel. They also will be able identify different grant vehicles intended to meet their specific research and training needs. Non-USA young investigators will hear about their specific opportunities. Finally, all participants will gain some perspective on various aspects of application preparation that affect review of their applications. Workshop Panelists: Jasenka Borzan, Ph.D. Scientific Review Officer (SRO) Neurobiology of Motivated Behavior (NMB) Study Section Center for Scientific Review (CSR) National Institutes of Health (NIH) Beth Babecki, M.A. Training Coordinator, Training Hub Division of Neuroscience and Behavior (DNB), NIDA Timothy H. Moran, PhD Paul R. McHugh Professor Executive Vice Chair Department of Psychiatry and Behavioral Sciences Johns Hopkins University School of Medicine Tim currently chairs the IPOD Study Section

3:30 - 5:30 PM	Calusa ABC
Symposium 1: A Taste for Chemical Sensing	

Chair(s): Alan Spector and Nuala Bobowski

3:30 **Oral Carbohydrate Sensing In Humans**
J LIM
Oregon State University, Corvallis, OR, United States

The primary function of taste is to identify substances that provide energy and/or electrolyte balance, while avoiding ingestion of toxic substances. Because starch is one of the major sources of energy that enables the body to perform its function, oral detection of starch, or its degradation products would be highly beneficial. However, the gustatory detection of starch is thought unlikely because of its molecular structure and size. Accordingly, glucose polymers (e.g., maltodextrin) have been used as tasteless caloric substances in studies of flavor-nutrient conditioning. Recently, we found the evidence that humans can taste starch hydrolysis products (i.e., maltooligosaccharides) and that such detection is independent of the sweet taste receptor, hT1R2/hT1R3. In this presentation, I'll discuss the role of salivary α-amylase in oral digestion of starch and illustrate perceptual evidence of gustatory detection of starch hydrolysis products. I'll also discuss sensory perception and possible transduction mechanisms of starch hydrolysis products. Overall, this presentation will highlight open questions about complex sensory mechanisms underlying oral carbohydrate sensing.

4:00 **Sweetness And Big Data: Molecular Substrates Of Consumer Liking**
DR REED
Monell Chemical Senses Center, Philadelphia, PA, United States

Here we examine two large datasets to understand the molecular substrates and real world significance of sweet taste. Although sweet and sweetness are almost universally liked, people differ, sometimes extremely so, in their ability to perceive and enjoy this taste quality and by extension, food and drink. The reasons for these differences among people are not clear but are probably due in part to perceptual or physiological differences that arise from genetic variation. Study results show that heritability of preferences for the sucrose solution and sweet foods range from low to moderate (h2 = 0.23 – 0.40). We report on the perception of several sweeteners in an Australian adolescent twin sample (n = 1757) and a U.S. adult twin sample (n = 686) using genome-wide association methods, finding suggestive associations for non-synonymous variants within ZNF502, KIF15, C9orf129 and KDM4A. Second we report on language use for 'sweet' and 'sweetness' in a data set of food reviews written by customers of an internet retailer (Amazon; N=568,454) to gauge the importance of this concept in human patterns of liking. Reviewers mention 'taste' in 30.3% of reviews and

sweetness in 10.3% of reviews, almost 10 times more often than 'saltiness' or the other taste qualities. Strategies for reducing sugar intake and sweet consumption need to consider inborn genetic differences and that for some people, sweetness is an indispensable feature that drives preference and liking.

4:30 **Communicating The Nutritional Value Of Sugar To Other Animals**

F ABU[1], J WANG[1], Y OH[1], J DENG[1], TA NEUBERT[1], GSB SUH[1,2]

[1]Skirball Institute of Biomolecular Medicine Neuroscience Institute Department of Cell Biology New York University School of Medicine, New York, NY, United States, [2]Department of Biological Sciences Korea Advanced Institute of Science and Technology, Daejeon, South Korea

Sweet-insensitive *Drosophila* mutants are unable to readily identify sugar. In presence of wild-type (WT) flies, however, these mutant flies demonstrated a marked increase in their preference to nutritive sugar. Real-time recordings of starved WT flies revealed that these flies discharge a drop from their gut end after consuming nutritive sugars but not non-nutritive sugars. We proposed that the drop may contain a molecule(s), named Calorie-Induced Secreted Factor (CIF), that serves as a signal to inform other flies about its nutritional value. Consistent with this, we observed a robust preference of flies for nutritive sugar containing CIF over nutritive sugar without CIF. Feeding appears to be a prerequisite for the release of CIF, given that fed flies did not produce it. Additionally, correlation analyses and pharmacological approaches suggest that the nutritional value rather than taste of the consumed sugar correlates strongly with the amount (or intensity) of the released CIF. We observed that the release of this attractant signal requires the consumption of macronutrients, specifically nutritive sugars and l-enantiomer essential amino acids (l-eAAs), but it is negligibly released when flies are fed non-nutritive sugars, unnatural d-enantiomer essential amino acids (d-eAAs), fatty acids, alcohol, or salts. Finally, CIF (1) is not detected by the olfactory system; (2) is not influenced by the sex of the fly; and (3) is not limited to one species of *Drosophila*.

5:00 **Sensing Mechanisms Of Water And Salt For Body Fluid Homeostasis**

YUKI OKA
California Institute of Technology, Pasadena, CA, United States

Body fluid homeostasis represents an important function to maintain the internal balance between water and salt. This regulation relies on the central sensing of internal water balance for appetite control, and the peripheral sensing of water and salt for consummatory decision. Thus, defining the molecular and neural basis underlying fluid detection at both peripheral and central levels is critical to understand the homeostatic regulation of fluid balance. In this talk, I will describe cellular logic of water and salt detection in the mammalian taste system using genetics and optogenetic manipulation. I also present our recent studies about the neural architecture for sprocessing internal water balance. The potential mechanisms how thirst and satiety are regulated by these neural circuits will be discussed.

3:30 - 5:30 PM	Calusa FGH
ORAL SESSION 3: The gut-brain axis	

Chair(s): Claire de la Serre and Charlene Diepenbroek

3:30 **Lateral Asymmetry Of Vagal Central Transynaptic Circuits**

A DE ARAUJO, W HAN, I DE ARAUJO, G DE LARTIGUE
JB Pierce/Yale, New Haven, CT, United States

Vagal afferent neurons (VAN) convey satiation information to relay circuits within the central nervous system, but the identity of the nuclei that process this incoming sensory information remains poorly characterized. **Method**: To address this, the cre-dependent anterograde transsynaptic tracing virus (H129ΔTK-TT-tdtomato) was injected into the left or right nodose ganglia (NG) of vGlut2^{Cre} mice. To map central synaptic circuitry from the gut, wildtype mice received injection of the cre-expressing retrograde virus (retroAAV-hSyn-BFP-cre) into the wall of the stomach and duodenum along with H129TKTT-tdTomato into the right NG. Perfused brains were collected 2-5 days post infection, sectioned and imaged by confocal microscopy. **Results** Infection was initially restricted to the dorsal vagal complex. After a few days, both the right and left NG injection labeled the dorsomedial and paraventricular hypothalamic nuclei, Bed nucleus of the stria terminalis, and parabrachial nucleus. Interestingly , reward nuclei only received inputs from the right NG. Gastric and duodenal innervating right NG similarly projected to the parabrachial nucleus, paraventricular nucleus of the hypothalamus and the substantia nigra. **Conclusion:** The central projections of right and left nodose ganglia map to overlapping but distinct circuits.

3:45 **Gut Vagal Sensory Signaling Regulates Hippocampus Function Through Multi-Order Pathways**

AN SUAREZ[1], TM HSU[2], AM CORTELLA[1], G DE LARTIGUE[3], SE KANOSKI[1]
[1]University of Southern California, Los Angeles, CA, United States, [2]University of Illinois at Chicago, Chicago, IL, United States, [3]Yale Medical School, New Haven, CT, United States

The vagus nerve is the primary means of neural communication between the gastrointestinal (GI) tract and the brain. Vagally-mediated within-meal GI signals, including gastric distension and intra-gastric nutrient infusion, activate the neurons in the hippocampus (HPC). However, the endogenous relevance of GI-derived vagal HPC communication is unknown. Here we explored the hypothesis that chronic disruption of gut-to-brain vagal tone via subdiaphragmatic vagotomy (SDV) negatively impacts HPC-dependent memory function in rats. Consistent with this hypothesis, SDV impaired performance in two HPC-dependent memory tasks involving processing of visuospatial stimuli: a spatial working memory task (modified Barnes' maze protocol) and a contextual episodic memory task (novel object in context protocol). To determine whether vagal afferents or efferents play a role in HPC-dependent memory function, we left efferents intact and eliminated 70% of vagal afferents through CCK-Saporin nodose injections and found the same impairment in spatial working memory and episodic memory. Consistent with the SDV- and CCK-Saporin-mediated HPC-dependent memory disruption, immunoblot analyses revealed reduced HPC neurotrophic and neurogenesis markers relative to controls. To determine the neural pathways connecting the gut to the HPC, we utilized monosynaptic and multisynaptic virus-based tracing methods to identify the medial septum as a relay connecting the medial nucleus tractus solitarius (where GI vagal afferents synapse) to dorsal HPC glutamatergic neurons. We conclude that endogenous GI-derived vagal sensory signaling promotes HPC-dependent memory function via a multi-order brainstem-septal pathway, thereby identifying a previously unknown role for the gut-brain axis in memory control.

4:00 **Body Weight Gain Does Not Predict Behavioral Sensitivity To Exogenous Cck, But May Influence Neural Activation In The Caudal Nucleus Of The Solitary Tract (Cnts).**

KD WALL[1], DR OLIVOS[2], L RINAMAN[1]
[1]Florida State University , Tallahassee, FL, United States, [2]University of Pittsburgh , Pittsburgh, PA, United States

When maintained on chow or high-fat diet (HFD), some rats eat larger meals and gain more BW than others, suggesting reduced sensitivity to endogenous satiety signals such as CCK. Exogenous CCK activates cFos within the cNTS, and prolactin-releasing peptide (PrRP) cNTS neurons may mediate CCK hypophagia. Here we examined whether BW gain over time is related to CCK-induced hypophagia and PrRP neural activation in adult male rats. After 2 wk on chow (13% fat) or HFD (45% fat), an inverse correlation between BW gain and CCK (1.0 ug/kg i.p.)-induced cNTS cFos was evident across all rats in both diet groups (R^2 =0.41, p=0.03). However, there was no effect of diet on total cNTS or PrRP activation, and PrRP neurons were similarly activated by i.p. saline and CCK (~40% for each). In a separate experiment, CCK hypophagia was examined in rats after 2 and 6 wk access to chow or HFD; suppression of 30 min dark-onset food intake did not differ between diet groups at either 2 or 6 wks, and was not correlated with BW gain in either diet group. CCK-induced cFos was examined after 7 wk access to chow or HFD. While there was no effect of diet

on overall cNTS cFos after CCK, activation of PrRP neurons was inversely correlated with 7 wk BW gain across both diet groups (R^2=0.46, p=0.02), and CCK activated fewer PrRP neurons in HFD- vs. chow-fed rats (29% vs. 41%; p=0.01). CCK differentially activated PrRP neurons (vs. saline) only in the second study, when rats were larger and more habituated to i.p. injections. We conclude that BW gain over time is not associated with behavioral sensitivity to CCK in either chow- or HFD-fed rats. While activation of PrRP neurons by CCK is related to BW gain, we are unable to conclude whether this relationship is consequential or causal.

4:15 **(Nita Award Winner) Nmda Receptors Contribute To Facilitation Of Vagal Afferent Synaptic Function In Leptin Receptor-Expressing Neurons Of The Nucleus Tractus Solitarius (Nts)**

DM NEYENS, H ZHAO, RC RITTER, SM APPELYARD
Washington State University, Pullman, WA, United States

The hindbrain nucleus of the solitary tract (NTS) is a site where vagally transmitted GI signals are integrated with descending central neural signals and circulating hormones. NTS injections of leptin reduce food intake and meal size, but the cellular mechanisms by which leptin does this are unknown. Work from our lab has shown that NTS NMDA receptors (NMDAR) maintain fidelity of vagal afferent synaptic transmission during high-frequency firing, as occurs during a meal. We have found that the majority of leptin receptor-expressing (LepR) NTS neurons co-express NMDA receptors. In other brain areas leptin has been shown to modulate NMDAR function. Therefore, we tested the hypothesis that leptin enhances NTS neuronal responses to vagal afferent stimulation by modulating NMDAR function. Using patch clamp recordings from acute horizontal brain slices, we measured changes in excitatory post-synaptic currents and synaptic throughput in LepR-expressing NTS neurons that receive vagal afferent input. We found that, in a subpopulation of LepR neurons, leptin increased the amplitude of vagally-evoked NMDAR currents during high-frequency solitary tract stimulation (130% ± 10%, n = 5/13). Leptin application also produced a 3-fold increase in the number of action potentials generated per vagal stimulation (5Hz) from 0.33 to 1.05 ± 0.17/stimulation ($p < 0.05$) in 7/11 neurons. The NMDAR antagonist DCPPene reduced throughput from 0.35 to 0.04 ± 0.02/stimulation ($p < 0.05$), and blocked the effect of leptin (DCP + leptin = 0.03 ± 0.02 APs per stim, n = 10). These data indicate that, in a subpopulation of LepR-expressing NTS neurons, leptin enhances responding to vagal input in an NMDAR-dependent fashion.

4:30 **Differential Contributions Of Nts And Ap Glp-1R Populations In Mediating The Food Intake-Suppressive Effects Of Liraglutide**

SM FORTIN[1], R LIPSKY[1,2], CG LIBERINI[1], T BORNER[2], R LHAMO[1], MR HAYES[1,2]
[1]Department of Psychiatry, University of Pennsylvania, Philadelphia, PA, United States, [2]Department of Biobehavioral Health Sciences, School of Nursing, University of Pennsylvania, Philadelphia, PA, United States

While the glucagon-like peptide-1 (GLP-1) receptor agonist liraglutide, is FDA-approved for the treatment of obesity, there is still much to be learned regarding the neuronal site of action and cellular, physiological and behavioral mechanisms that underlie its food intake and body weight-suppressive effects. Previous work has shown that peripherally administered liraglutide acts in part through central GLP-1 receptors (GLP-1Rs) in both the hypothalamus and hindbrain. Here, we extend findings supporting a role for hindbrain GLP-1Rs in mediating the anorectic effects of liraglutide in the rat. IHC analyses confirm that liraglutide (50 mg/kg) increases c-Fos activity in neurons within the area postrema (AP) and nucleus tractus solitarius (NTS) compared to vehicle. To dissociate the contribution of GLP-1Rs in the AP and the NTS, we next examined the effects of liraglutide (25 and 50 mg/kg) in both NTS AAV-shRNA-driven GLP-1R knockdown and AP-lesioned animals. Knockdown of NTS GLP-1Rs, but not surgical lesioning of the AP, attenuated the anorectic and body weight-suppressive effects of liraglutide. Ongoing fiber photometry studies are exploring NTS neural activation by liraglutide. Our data highlight the NTS, but not the AP, as a site of action for the GLP-1R-mediated food intake and body weight-suppressive effects liraglutide.

4:45 **Depleting Amylin Signaling In Pomc Neurons In Mice Alters Glucose And Energy Metabolism**

B. COESTER, T.A. LUTZ, C. LE FOLL
Institute of Veterinary Physiology, Vetsuisse Faculty, University of Zurich , Zurich, Switzerland

In addition to amylin's effect on food intake via the area postrema, amylin also acts specifically on ARC POMC neurons via the ERK signaling pathway. This study assessed the physiological role of amylin signaling in POMC neurons using an inducible mouse model by specifically depleting CTR, one of the amylin receptor sub-units. 4 groups of mice were assessed: $CTR^{fl/fl}$ POMC-Cre:$ER^{T2+/+}$ oil-treated (Oil-ctrl), $CTR^{fl/fl}$-POMC-

Cre:ER$^{T2+/+}$ tamoxifen-treated (Tx-ctrl), CTR$^{fl/fl}$-POMC-Cre:ER^{T2Tg+} oil-treated (Oil-cre) and CTR$^{fl/fl}$-POMC-Cre:ER^{T2Tg+} tamoxifen-treated (Tx-cre = POMC^{CTR-KO}). From 5 to 6 wk old, mice were injected for 5 days with 150 µg/kg of Tx. In a first cohort of chow-fed mice, effects of amylin (50, 500 µg/kg), salmon calcitonin (sCT, 10 µg/kg) and leptin (5 mg/kg) on food intake were assessed. In a second (chow diet) and third cohort (45% high fat diet-HFD; Research Diet D12451), weekly body weight, food intake, OGTT, ITT, indirect calorimetry, body temperature and activity were assessed. On chow diet, POMC^{CTR-KO} mice gained more weight (+50%, P< 0.05) than the other groups and food intake was also increased by 13% (P< 0.05) as compared to Tx-ctrl mice. POMC^{CTR-KO} mice were glucose intolerant and less active as compared to Tx-ctrl mice. sCT was unable to increase EE as compared to Tx-ctrl mice. Furthermore, amylin and sCT decreased food intake similarly in all groups suggesting that amylin signaling in POMC neurons is not a major regulator of food intake. On 45%HFD, POMC^{CTR-KO} male mice body weight and food intake were similar to the other groups and their glucose tolerance was decreased compared to Tx-Ctrl mice (P< 0.05). These results suggest that amylin signaling in POMC neurons seems to participate in the regulation of body weight and energy homeostasis.

5:00 **Associations Between Ghrelin And Leptin And Neural Food-Cue Reactivity In A Fasted And Sated State**

MCM WEVER[1], L CHARBONNIER[1], D CRABTREE[2], W BUOSI[2], A GIANNOPOULOU[3], F VAN MEER[1], O ANDROUTSOS[3], AM JOHNSTONE[2], Y MANIOS[3], PAM SMEETS[1]

[1]University Medical Center Utrecht, Utrecht, Netherlands, [2]University of Aberdeen, Aberdeen, United Kingdom, [3]Harokopio University Athens, Athens, Greece

Food-cue reactivity is affected by many factors, such as hunger state and BMI. Two key appetite-related hormones are ghrelin and leptin, which are involved in both homeostatic and hedonic eating. So far, studies linking ghrelin and leptin with brain responses to food cues are sparse and show inconsistent results. We examined the associations between ghrelin and leptin levels and neural food cue reactivity in a fasted and sated state.
Data from 130 participants were analyzed (mean age=51.9 y; mean BMI=26.9 kg/m2). They performed a food image viewing task during fMRI, after an overnight fast and after a standardized meal. In this task, they watched high-energy (HE), low-energy (LE) and non-food images. Blood samples were drawn prior to the viewing task.
Preliminary results are as follows: there was a positive correlation between ghrelin and food vs non-food viewing in the left angular gyrus and left cuneus in the fasted state, and a positive correlation between ghrelin and brain activation in the left parahippocampal gyrus in the sated state. Furthermore, the difference in ghrelin levels between the fasted and the sated state was positively correlated with the difference in food vs non-food activation in the left inferior parietal gyrus. Leptin correlated positively with brain activation in the left caudate during HE vs LE image viewing in the sated state. However, this effect was no longer significant when BMI was included in the model.
In conclusion, ghrelin is associated with greater neural food-cue reactivity, with a modulating effect of hunger state. Leptin only covaries with brain reactivity during satiety, but this may reflect heightened reactivity in overweight individuals despite being sated.

5:15 **Effects Of Oat B-Glucan Consumption At Breakfast On *Ad Libitum* Eating, Appetite, Glycemia, Insulinemia And Glp-1 Concentrations In Healthy Subjects**

SMM ZAREMBA[1], IF GOW[1], S DRUMMOND[1], JT MCCLUSKEY[1], RE STEINERT[2, 3]

[1]Dietetics, Nutrition & Biological Sciences, Queen Margaret University, Edinburgh, United Kingdom, [2]DSM Nutritional Products Ltd., R&D Human Nutrition and Health, Basel, Switzerland, [3]Department of Surgery, Division of Visceral and Transplantation Surgery, University Hospital Zürich, Zurich, Switzerland

There is evidence for oat β-glucan to lower appetite and *ad libitum* eating, however, not all studies are consistent, and the underpinning mechanisms are not entirely understood. We investigated the effects of 4 grams high molecular weight (MW) oat β-glucan on *ad libitum* eating, subjective appetite, glycemia, insulinemia and plasma GLP-1 responses in 33, normal-weight subjects (22 female/11 male, mean age (yrs): 26.9 ± 1.0, BMI (kg/m^2): 23.5 ± 0.4). The study followed a double-blind, cross-over design with subjects fed two different test breakfasts with and without oat β-glucan on two different days in random order, followed by an *ad libitum* test meal. Blood samples and ratings for subjective appetite were collected postprandially at regular time intervals. Oat β-glucan increased feelings of fullness (p=0.046) and satiety (p=0.021), however, there was no effect on energy and amount eaten at the *ad libitum* test meal. There was a treatment by time interaction for plasma GLP-1, plasma insulin and blood glucose. GLP-1 was significantly reduced at 90 min (p=0.021), blood glucose at 30 min (p=0.008) and plasma insulin at 30 and 60 min (p=0.002 and 0.017, respectively) following the oat β-glucan breakfast when compared with the control breakfast. High MW oat β-glucan at 4 grams lowers appetite but not *ad libitum* eating and beneficially modulates postprandial glycaemia associated with a small decrease in plasma GLP-1.

5:30 - 7:30 PM	Calusa DE
POSTER SESSION I	

P1 **High-Fat Diet Changes Drinking Behavior And Drinking Response To Glp-1 Agonist Exendin-4**

KL VOLCKO, QE CARROLL, S KAUR, D DANIELS
Behavioral Neuroscience Program, Department of Psychology, University at Buffalo SUNY, Buffalo, NY, United States

Glucagon-like peptide-1 (GLP-1) reduces food and water intake. Previous research found that the hypophagic effect of the GLP-1 agonist exendin-4 (Ex4) is attenuated in rats maintained on a high-fat diet (HFD). To test if this finding extends to the effects of Ex4 on water intake, we maintained male Sprague-Dawley rats on a low-fat diet (LFD) or HFD (60%) for five weeks, during which body weight (BW) and 24-hour food and water intakes were recorded. We then measured dark-phase drinking, in the absence of food, after injection of 0, 1 and 3μg/kg Ex4 (ip). Finally, we tested the effect of 1μg/kg Ex4 on drinking caused by subcutaneous (sc) hypertonic saline in HFD and LFD rats. We found that HFD rats consumed more calories but drank less water than did LFD rats, when the data were normalized by BW. Analysis of licking patterns found that the difference in water intake was a function of licking burst size, and not burst number, suggesting a role for altered orosensory feedback. Interestingly, when HFD rats were retrospectively divided into high and low weight gain groups, we found no sub-group differences in water intake, indicating that the differences in drinking between rats on HFD and LFD were a function of the diet, and not due to BW differences. Although experiments are ongoing, our preliminary analysis suggests that HFD rats were less responsive to Ex4 in dark-phase intake tests, but we found no effect of diet on the anti-dipsogenic effect of Ex4 on drinking after sc hypertonic saline. Together, these results indicate that diet alters drinking behavior, but in a direction that is not consistent with the cause being an attenuation of endogenous GLP-1, and that HFD reduces GLP-1-induced hypodipsia only under some circumstances.

P2 **Knockdown Of Glucagon-Like Peptide-1 Receptor Increases Water Intake In Rats**

D.J. BRAKEY[1], K.L. VOLCKO[1], Q.E. CARROLL[1], M.R. HAYES[2], D. DANIELS[1]
[1]Behavioral Neuroscience Program, Department of Psychology, State University of New York at Buffalo, Buffalo, NY, United States, [2]Department of Psychiatry, University of Pennsylvania, Philadelphia, PA, United States

Glucagon-like peptide-1 (GLP-1) and GLP-1 receptor (GLP-1R) agonists decrease water intake, independent of any effect on food intake. More evidence, however, is needed to evaluate the role of endogenous GLP-1R signaling. Accordingly, the goal of this study was to determine if knockdown of GLP-1R in the *nucleus tractus solitarius* (NTS) influences drinking behavior. To this end, adult male Sprague Dawley rats were implanted with chronic indwelling cannula aimed at the medial NTS. After measuring baseline food and water intakes, rats were injected with either an AAV that expresses GFP and shRNA to knockdown GLP-1R, or a control AAV expressing GFP. Overnight food and water intakes then were measured once a week for five weeks. Preliminary analyses indicate that rats with NTS GLP-1R knockdown drank, ate, and weighed more than controls. The timing of these effects differed, however, in that changes in water intake and body weight appeared to occur before changes in food intake were observed. Planned studies will evaluate the behavioral and neural responses to injections of a GLP-1R agonist, will test for differences in response to acute dipsogenic treatment and will provide a postmortem screen for properly placed virus injections. Although these conclusions are preliminary, and based on sample sizes that continue to grow as new cohorts are added to the study, the results collectively provide further support for the overarching hypothesis that water intake is controlled, at least in part, by endogenous GLP-1R signaling. Support provided by DK107500 (DD).

P3 **Evaluating Function Of Angiotensin Sensitive Neurons Of The Subfornical Organ In Body Fluid Homeostasis.**

AR ALLEYNE, KM CAHILL, MD SMELTZER, Y TAN, AD DE KLOET, EG KRAUSE
University of Florida, Gainesville, FL, United States

Circulating angiotensin II elicits behavioral and physiological responses to decreased blood pressure or hypovolemia by activating angiotensin type-1a receptors (AT1aR) in circumventricular organs that lack a blood brain barrier. In particular, the subfornical organ (SFO) contains neurons that express AT1aR and are implicated in the maintenance of body fluid homeostasis. This study used mice with Cre recombinase expression directed to the AT1aR gene to functionally phenotype neurons in the SFO that express AT1aR. Initial studies combined genetic reporting with RNAscope in situ hybridization to reveal that the majority of AT1aR neurons in the SFO are glutamatergic. Next, Cre-inducible adenoassociated virus that expresses channelrhodopsin-2 (ChR2) or enhanced yellow fluorescent protein (eYFP) was delivered into the SFO of AT1aR-Cre mice, and subsequently, a chronic dwelling fiber optic was implanted. Relative to controls expressing eYFP, in vivo optogenetic stimulation of AT1aR neurons in the SFO significantly increased water and 0.3M NaCl consumption. Interestingly, optical excitation of the same population of neurons also significantly elevated plasma levels of corticosterone. Taken together, these results suggest that neurons in the SFO that synthesize AT1aR drive water and sodium intake as well as activation of the hypothalamic-pituitary-adrenal axis.

P4 **Role Of Paraventricular Thalamic Glucagon-Like Peptide-1 Receptor Signaling On Alcohol Intake Behaviours**

ZY ONG, GP MCNALLY
School of Psychology, University of New South Wales, Sydney, Australia

Alcohol use disorder (AUD) is a serious health concern, yet current treatments for this disorder are limited with modest efficacy. Recent preclinical studies show that systemic glucagon-like peptide-1 (GLP-1) analogues robustly reduce alcohol intake. We further showed that the effects of GLP-1 receptor (GLP-1R) signaling on alcohol intake are mediated, in part, through its receptors in the paraventricular thalamus (PVT). However, whether PVT GLP-1R signaling affects other aspects of dysregulated alcohol drinking behaviours relevant to AUD, including relapse, is unknown. Here, we test the hypothesis that PVT GLP-1R signaling reduces alcohol self-administration, reacquisition/relapse, and the motivation to work for alcohol in rodents. Results show that intra-PVT delivery of GLP-1R agonist (Exendin-4 (Ex4); 12.5ng/100nL) had no effect on self-administration or the motivation to work for 10% alcohol. Nonetheless, Ex4 delivered specifically to the anterior PVT (aPVT), but not the posterior PVT (pPVT), reduced relapse during reacquisition by ~50%, with a strong trend towards statistical significance (alcohol deliveries: Veh 33±7.9, Ex4 16.6±3.3; n=5 or 7; P=0.06). Furthermore, the dose of Ex4 used is without effect on food intake, body weight, and is not associated with malaise. Together, these data suggest a role for aPVT GLP-1R signaling in reducing alcohol intake specifically during relapse and thus in promoting abstinence. Current experiments expand on these findings and examine the downstream targets mediating the effects of aPVT GLP-1R signaling on relapse.

P5 **Potential Mechanisms Mediating The Effects Of Contingent Availability Of A Palatable Diet On Alcohol Drinking**

S VILLAVASSO[1], J CLEVELAND[1], JF DAVIS[2], S SIROHI[1]

[1]Laboratory of Endocrine and Neuropsychiatric Disorders, Division of Basic Pharmaceutical Sciences, College of Pharmacy, Xavier University of Louisiana, New Orleans, LA, United States, [2]Department of Integrative Physiology & Neuroscience, Washington State University, Pullman, WA, United States

We have recently reported that an intermittent exposure to a nutritionally complete high-fat diet (HFD) reduces alcohol drinking in rats. The present study evaluated central neurotransmitter receptors gene expression to elucidate the underlying neurobiological mechanism of HFD-induced reduced alcohol drinking in male Long Evans rats. We also examined the impact of a high-sugar diet (HSD) on alcohol drinking. Rats (n=6-15/group), received intermittent (24 hrs twice a week on Tue and Thru) access to HFD, HSD or normal chow (controls) for two-weeks. No baseline differences in the body weight, water, or food intake existed. Normal chow and water were available ad libitum to all rats and food intake was recorded. Following initial two-weeks of palatable diets (PD) exposure, rats were allowed to drink ethanol (20% v/v) on the chow-only access days (Mon, Wed, Fri) and intermittent HFD/HSD cycling continued. Brains were isolated at the end of the study and hypothalamic neurotransmitters receptors gene expression (RT^2 Profiler PCR array) was evaluated. Rats in the PD access groups developed a binge/compensate pattern of food consumption. A significantly reduced alcohol drinking was observed in both Int-HFD/HSD groups compared to chow controls. Hypothalamic expression of muscarinic (*Chrm4*), GABAergic (*Gabra2, Gabrb1, Gabrb3, Gabrg2*) and glutamatergic (*Gria2*) receptors transcripts were significantly ($p< 0.05$) increased in the Int-HFD rats compared to controls. These data reveal that a palatable food contingency is effective in attenuating alcohol drinking and alterations in the central inhibitory neurotransmission may mediate these effects.

P6 **An Amylin Analogue Attenuates Drinking Behaviours In Animal Models Of Alcohol Use Disorder, But Does Not Affect Self-Administration Of A Palatable Beverage In Rats**

AL KALAFATELI[1], D VALLOF[1], G COLOMBO[2], I LORRAI[2], P MACCIONI[2], E JERLHAG[1]

[1]Institute of Neuroscience and Physiology, Department of Pharmacology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, Gothenburg, Sweden, [2]Neuroscience Institute, Section of Cagliari, National Research Council of Italy, Monserrato (CA), Italy, Cgliari, Italy

Reward induced by food and addictive drugs, like alcohol, involve common neurochemical mechanisms. They activate areas of the mesolimbic dopamine system, which consists of dopaminergic neurons projecting from the ventral tegmental area (VTA) to nucleus accumbens (NAc). This suggests that gut-brain hormones, like amylin, which control appetite and energy balance, could be involved in reward regulation. We investigated whether salmon calcitonin (sCT), an amylin receptor agonist and amylin analogue, affects alcohol reward and intake. We showed that repeated sCT administration attenuated alcohol, as well as food intake in 25 Wistar rats. Additionally, acute sCT administration reduced operant alcohol self-administration (fixed ratio schedule of reinforcement) in 36 selectively bred Sardinian alcohol-preferring rats, but did not alter operant self-administration (progressive ratio schedule of reinforcement) of a highly palatable chocolate-flavoured beverage in 36 Wistar rats. Moreover, acute administration of sCT prevented relapse-like drinking in the “alcohol deprivation effect” model in 20 Wistar alcohol-experienced rats. Collectively, our data suggest that amylin signalling is involved in reward regulation and may differentially affect drug and food reward.

P7 **Brief-Access To Ethanol Or Quinine Facilitates Subsequent Ethanol Consumption.**

GC LONEY, PJ MEYER
The State University of New York at Buffalo, Buffalo, NY, United States

The taste of alcohol is a potent indicator of concentration and serves as the most proximal cue to its reinforcing, pharmacological actions. Behavioral and neurophysiological studies have indicated that both humans and rodents treat alcohol as if it elicits both bitter- and sweet-like taste qualities and genetic analyses have revealed an association between bitter-receptor haplotypes and alcohol acceptance. Here, we systematically examined the predictive role of sensitivity to bitter tasting stimuli on alcohol acceptance in male rats. First, we demonstrate a positive correlation between hedonic licking to the bitter stimulus quinine and ethanol in randomized, brief-access licking trials. Next, we show that brief, antecedent exposure to quinine resulted in increased acceptance of subsequently presented ethanol in a concentration-dependent manner. Together, these results indicate that sensitivity to suprathreshold concentrations of quinine is predictive of acceptance of concentrated ethanol in naïve rats and, furthermore, that tasting quinine improved acceptance of ethanol through successive positive contrast. Finally, we examined the impact of previous ethanol exposure on acceptance of ethanol taste and, ultimately, subsequent free-access consumption. Repeated, brief-exposures to ethanol resulted in a significant rightward shift in acceptance of the taste as well as significantly facilitated total ethanol consumption. In summary, we propose that sensitivity to the aversive, bitter-like qualities of ethanol is a deterrent to consumption of ethanol and may serve as a barrier to drinking initiation.

P8 **Neuromedin U Regulates Reinforcing Properties Of Alcohol And Intake Of Palatable Food In Rodents Via The Mesolimbic Dopamine System**

D VALLöF, AL KALAFATELI, E JERLHAG
Institute of Neuroscience and Physiology, Department of Pharmacology, The Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden

In contrast to the common view of the function of gut-brain peptides, such as neuromedin U (NMU), to regulate food intake and appetite a novel role in reinforcement mediation has been implied. Given that the anorexigenic effects of NMU are mediated via NMU2 receptors, which are expressed in reward related areas in the brain, we hypothesize that these receptors in reward related areas might regulate alcohol reinforcement and intake of palatable food. The present series of experiments were designed to evaluate the effect of local administration of NMU, into the nucleus accumbens (NAc), the ventral tegmental area (VTA) or the laterodorsal tegmental area (LDTg) on alcohol-induced locomotor stimulation, conditioned place preference (CPP) as well on palatable food intake in mice. In addition, the effect of NMU into NAc on alcohol consumption was evaluated in rats. Local administration of NMU into the NAc significantly attenuated alcohol-induced locomotor stimulation (n=40), CPP (n=14) and reduced intake of palatable food (n=30) in mice as well as reduced alcohol intake (n=14) in rats. Intra-VTA NMU administration had no effect on alcohol-induced locomotor stimulation (n=60), CPP (n=16) or intake of palatable food (n=30). Local administration of NMU into the LDTg had no effect on alcohol-induced locomotor stimulation (n=64), CPP (n=16) or intake of palatable food (n=30). However, intra-VTA (n=30) or intra-LDTg (n=30) NMU administration reduced the intake of normal chow in mice.
Collectively, these data suggest that intra-NAc NMU administration, rather than intra-VTA and intra-LDTg, have an effect on alcohol reinforcements and intake of palatable food.

P9 **Brain Responses To Anticipation And Consumption Of Beer With And Without Alcohol**

PAM SMEETS, C DE GRAAF
Wageningen University, Wageningen, Netherlands

Alcoholic beverages are very popular around the world, due to their alcohol-derived reward value. Also, alcohol constitutes a source of calories. Non-alcoholic beer may be a low-calorie thirst-quenching alternative for sugar sweetened beverages. Brain reward responses to beer and non-alcoholic beer have not been compared. Specifically, it is unknown in how far the flavor of beer, rather than the sensory perception of alcohol per se, is associated with reward. Therefore, we investigated how the brain responds to anticipation to and consumption of beer, while covertly delivering beer with or without alcohol. Healthy men (n=21, age 25.1 ± 3.3 y, body mass index 22.5 ± 1.8 kg/m^2) who were regular beer drinkers were scanned using functional MRI. Participants were exposed to visual cues signaling delivery of a 10-ml sip of chilled beer or carbonated water (control) and subsequent sips of beer with or without alcohol or water (control). The beer cue elicited less activation than the control cue in the primary visual cortex, supplementary motor area (reward region) and bilateral inferior frontal gyrus/frontal operculum. During tasting, there were no significant differences between the two beers. Taste activation after swallowing was significantly greater for alcoholic than for non-alcoholic beer in the inferior frontal gyrus/anterior insula and dorsal prefrontal cortex (superior frontal gyrus). This appears to be due to sensory stimulation by ethanol rather than reward processing. In conclusion, we found no differences in acute brain reward upon consumption of beer with and without alcohol, when presented in a context where regular alcoholic beer is expected. This suggests that in normal regular consumers beer flavor rather than the presence of alcohol drives the consumption experience.

P10 **Activation Of Dorsomedial Hypothalamic Neurons Promotes Physical Acivity And Decreases Food Intake And Body Weight In Leptin Receptor-Deficient Rats**

N ZHANG[1,2], L YANG[1], L GUO[2], S BI[1]

[1]Department of Psychiatry and Behavioral Sciences, Johns Hopkins University SOM, Baltimore, MD, United States, [2]Department of Psychiatry, West China Hospital, Chengdu, China

Previous reports have shown that running wheel activity or voluntary exercise prevents hyperphagia and obesity in some animal models of obesity, but such effects seem only minimal in obese animals lacking leptin or leptin receptors. The mechanism underlying this ineffectiveness remains unclear. Here, we report the action of neuronal activation in the dorsomedial hypothalamus (DMH) in modulating physical activity, food intake and body weight in leptin receptor (LepR)-deficient rats. Sedentary LepR-deficient rats became hyperphagic and gained body weight rapidly. Although they had access to running wheels, their running activity was low and their food intake and body weight were unchanged. Determinations of hypothalamic gene expression revealed that lepR-deficient rats had increased expression of *Npy* and decreased expression of *Pomc* in the arcuate nucleus (ARC). Both ARC *Npy* and *Pomc* expression were further altered in LepR-deficient rats under running and pair-fed conditions, indicating that both genes are appropriately regulated in response to increased energy demands. c-Fos immunohistochemistry revealed that running activity elevated the number of c-Fos positive cells in the DMH of intact rats, but such effects were not found in LepR-deficient rats. Using adeno-associated virus-mediated expression of the designer receptors hM3D(Gq) in the DMH of LepR-deficient rats, we found that chemogenetic stimulation of neurons in the DMH significantly increased their running activity and reduced their food intake and body weight. Together, these results demonstrate that activation of DMH neurons promotes physical activity and decreases food intake and body weight, suggesting that exercise-induced reductions of food intake and body weight are likely via DMH neural pathway.

P11 **Role Of Bmp8B In Trpv1-Mediated Thermogenic Mechanisms**

P BASKARAN, B THYAGARAJAN
University of Wyming, Laramie, WY, United States

Diet-induced obesity suppresses the thermogenic functions of brown fat and progressively causes whitening of brown adipose tissue (BAT). Activation of transient receptor potential vanilloid subfamily 1 (TRPV1) protein expressed on WAT and BAT by capsaicin (a selective TRPV1 agonist) stimulates the browning of WAT and BAT thermogenesis to promote weight loss in mice. Bone Morphogenetic Protein 8B is a very important secretory molecule which regulates thermogenesis. Capsaicin enhanced the expression of thermogenic bone morphogenetic protein b8 (BMP8b) in the WAT and BAT and increased its secretion in the blood of wild type but not in $TRPV1^{-/-}$. Also, capsaicin stimulated BMP8b release from cultured brown adipocytes in vitro and primary adipocytes isolated from inguinal fat from WT mice. BMP8b secretion was associated with an increase in SMAD 1 phosphorylation and PPARa expression in BAT. BMP8b upregulation in adipose tissue mediated by capsaicin is parallel to the signal transduction cascade activated by TRPV1. Accordingly, capsaicin activated metabolically important sirtuin-1, PPARa, PPARg coactivator 1a (PGC1a), PRDM-16, and UCP-1 in the BAT of wild type and $BMP8b^{-/-}$ but not in $TRPV1^{-/-}$ mice. Further, indirect calorimetric measurements suggest that capsaicin increased the respiratory quotient and heat production in the wild type but not in $TRPV1^{-/-}$ and $BMP8b^{-/-}$ mice. Our data thus suggest that the anti-obesity effect by TRPV1 activation involves the thermogenic protein BMP8b.

P12 **Monosynaptic Inputs To Hypothalamic Trpv1-Expressing Neurons**

LD DESMOULINS[1], A ZSOMBOK[1,2]

[1]Department of Physiology, School of Medicine, Tulane University, New Orleans, LA, United States, [2]Tulane Brain Institute, New Orleans, LA, United States

Transient Receptor Potential Vanilloid type 1 (TRPV1) is a ligand-gated nonselective cation channel associated with the regulation of energy homeostasis and cardiovascular functions. Acute stimulation of TRPV1 has been shown to improve glucose homeostasis by decreasing food intake, lower blood glucose by increasing insulin secretion, or trigger hypothermia. TRPV1 is expressed in the hypothalamus, a brain area involved in the regulation of energy homeostasis; however, the TRPV1-related neuronal network remains to be determined. Since TRPV1 is associated with energy homeostasis, we tested the hypothesis that TRPV1-expressing ($TRPV1^{+}$) neurons receive inputs from brain nuclei involved in the regulation of homeostatic functions. Rabies guided monosynaptic circuit-mapping was used to identify direct connections to hypothalamic $TRPV1^{+}$ neurons. Pseudo-typed rabies virus coupled with helper viruses (AAV-EF1a-Flex-TVA-mCherry + AAV-CA-Flex-RG.ape + EnvA-RVdG-GFP) was injected into the hypothalamus of $TRPV1^{Cre}$ mice to label the TRPV1-related network. First order $TRPV1^{+}$ (starter) neurons were located in the dorsomedial and posterior hypothalamus (DMH/PH). These starter neurons received monosynaptic inputs from the preoptic area, the lateral hypothalamus, the lateral periaqueductal gray and the mammillary nucleus, as well as the DMH and PH. These brain areas are known for their implication in the regulation of food intake, glucose metabolism, thermogenesis and cardiovascular functions. Our findings suggest that TRPV1-expressing DMH/PH neurons receive inputs from a variety of nuclei involved in the regulation of homeostatic functions; however, further studies are required to reveal the physiological role of hypothalamic TRPV1-expressing neurons *in vivo*.

P13 **Hypothalamic *Zinc Finger And Btb Domain Containing 16* (*Zbtb16*) Contributes To Cold-Adaptive Increase In Energy Expenditure And Food Intake**

H CHENG, SJ PABLICO, R ZHANG, E QUALLS-CREEKMORE, H MUNZBERG, S YU
Pennington Biomedical Research Center, Baton Rouge, LA, United States

Environmental temperature is a strong modulator of both energy expenditure and intake, and the hypothalamus is essential in governing temperature-dependent metabolic and behavioral responses. We discovered that *Zbtb16* is mainly expressed in the paraventricular (PVH) and arcuate (ARC) nuclei of the hypothalamus and that its expression is highly induced by ambient cold temperature in mice. We tested whether *Zbtb16* upregulation is critical for cold-adaptive increase in energy expenditure and food intake. When *Zbtb16* expression in the PVH was suppressed by viral expression of siRNA, cold-evoked thermogenesis was abated by 35% (control siRNA, n=4; *Zbtb16* siRNA, n=6, $p < 0.01$), while its knockdown in the ARC resulted in reduced night time food intake by 18% (control siRNA, n=4; *Zbtb16* siRNA, n=7; $p < 0.01$). Consistent with these phenotypes, some Zbtb16-expressing neurons (Zbtb16 neurons) in the PVH were labeled with pseudorabies virus injected in brown adipose tissue (BAT), suggesting its involvement in BAT thermogenesis. In the ARC, *Zbtb16* expression is highly enriched in agouti-related neuropeptide (Agrp) neurons, while its expression in proopiomelanocortin (POMC) neurons is scarcely observed. Furthermore, chemogenetic activation of Zbtb16-expressing neurons in the PVH and the ARC increased 2hr energy expenditure and food intake, respectively (in the PVH, control, n=9; hM3Dq, n=3; $p < 0.01$; in the ARC, PBS, n=4; CNO, n=4; $p < 0.01$). These results together indicate that *Zbtb16* might enhance the activity of Zbtb16 neurons. In summary, our study supports that *Zbtb16* is a cold-induced transcriptional regulator that may be important for cold-adaptive increase in energy expenditure and food intake.

P14 **Acute Blockade Of Pac1R-Dependent Signaling In The Ventromedial Nuclei Of The Hypothalamus (Vmn) Inhibits The Behavioral And Cellular Actions Of Leptin.**

MM HURLEY, EM HESS, B MAUNZE, MM FRENKEL, ME BLOCK, CA LAMBERTON, NS PATEL, Z COOPER, R MCCOY, T DABRA, W CONLEY, MJ REILLY, S CHOI
Marquette University , Milwaukee, WI, United States

Pituitary adenylate cyclase-activating polypeptide (PACAP) microinjected into the rat ventromedial nucleus of the hypothalamus (VMN) decreases food intake, body weight and increases activity as well as thermogenesis through the PACAP receptor, PAC1R. Interestingly, leptin microinjected into the VMN produces nearly identical behavioral changes to that of PACAP. In the current study, we examine whether leptin and PACAP signaling interact in the VMN to regulate behavior and energy homeostasis. To determine whether leptin actions are dependent on PACAP signaling, we antagonized PAC1R prior to leptin administration in the VMN and measured subsequent changes in food intake, body weight and core temperature. Antagonizing PAC1R (using PACAP 6-38) in the VMN prevented leptin induced suppression of food intake, body weight and stimulation of thermogenesis. Moreover, PACAP alone also increased STAT3 phosphorylation and SOCS3 mRNA expression in the VMN suggesting that PACAP activates the same cellular cascade as leptin. Interestingly, PACAP and leptin each increase BDNF mRNA in the VMN while pretreatment with PACAP 6-38 blocked the increase by both peptides. Fluorescent *in situ* hybridization revealed that VMN PAC1Rs are co-localized with leptin receptors. We conclude that blockade of PAC1R *specifically in the VMN* prevents leptin-induced hypophagia and cellular signaling cascade. All data were analyzed by ANOVA (repeated measures when appropriate) or Students t-test.

P15 **Hypothalamic Nitric Oxide Production Is Increased In Satiated Vs. Hungry Rats: Further Support For A Role Of No In Satiety**

N HAZUT[1,2], K RAPPS[1,2], A WELLER[3,2], AJ SUSSWEIN[1,2]
[1]The Mina and Evrard Faculty of Life-Sciences, Bar-Ilan University, Ramat-Gan, Israel, [2]The Gonda Brain Research Center, Bar-Ilan University, Ramat-Gan, Israel, [3]The Psychology Department, Bar-Ilan University, Ramat-Gan, Israel

Previous data have shown that nitric oxide (NO) mediates some of the orexigenic effects of ghrelin and PYY, and therefore it is “known” that NO excites feeding. However, we have recently found that NO is an inhibitor of feeding when rats are satiated, but nonetheless occasionally snack chow. In this condition, treatment with L-arginine (400 mg/kg and 150 mg/kg, i.p) the precursor from which NO is synthesized, inhibited snacking on chow. Thus, NO may have inhibitory effects in satiated animals. NO that inhibits feeding is likely to be released as a result of satiating signals. NO inhibition with the nitric oxide synthase blocker L-NAME increased feeding by increasing the number of feeding bouts, and L-arginine inhibited feeding by decreasing the number of feeding bouts. In order to discover which brain areas are involved in the process of NO inhibition of feeding, NADPH diaphorase staining was performed on brains of satiated and hungry rats. Our hypothesis was that more NO is released in brain areas that are related to satiety and feeding (i.e, ARC.n, LH and VMH) of satiated rats when compared to the same brain areas of hungry animals. Using the cell counting software, *Image J*, we discovered significant increases in NO producing cells ($p< 0.05$) in the Lateral Hypothalamus (LH),and in Ventro-medial part of the Hypothalamus (VMH) in satiated animals, with respect to hungry animals. These findings show that the inhibitory effects of NO in satiated

animals involves several areas of the hypothalamus related to feeding in the. Further experiments are needed to discover the full mechanism of NO inhibition of feeding.

P16 **Impact Of Obesity-Genes On The Human Hypothalamus**

A V WITTE[1], K THOMAS[1], F BEYER[1], M SCHOLZ[2], S SCHINDLER[3], P SCHöNKNECHT[3], A VILLRINGER[1]

[1]Max Planck Institute of Human Cognitive and Brain Sciences, Department of Neurology, Leipzig, Germany, [2]Institute for Medical Informatics, Statistics and Epidemiology, Leipzig, Germany, [3]University of Leipzig, Faculty of Medicine, Clinic and Policlinic of Psychiatry and Psychotherapy, Leipzig, Germany

Obesity is a complex multigenic trait and has been linked to abnormal functionality of homeostasis brain networks (Schwartz 2000). In patients, volumetric changes of the hypothalamus correlated with changes in body mass index and eating behaviour (Gorges 2017), and higher grey matter volume in the hypothalamus was associated with higher trait hunger in healthy adults (Yao 2016). Whether obesity-genes affect the human hypothalamus has however not been addressed. We therefore aimed to determine the effects of obesity-risk alleles on the human hypothalamus using a segmentation protocol for *in vivo* magnetic resonance imaging (MRI) of the hypothalamus. In total, 338 healthy adults (162 women, 176 men, 20-80 years) of the LIFE study (Loeffler 2015) who underwent multimodal MRI, anthropometric assessments and fasting blood draw were included. Volume and mean diffusivity (MD) of the hypothalamus derived by segmentation on T1-weighted 3T MRI using a customized unified segmentation algorithm (Schindler 2013) and co-registration of diffusion-tensor images. Semi-manual segmentation showed good spatial agreement (DSC 0.88-0.94) and mean hypothalamus volume was higher in males compared to females (adjusted for age, $F = 11.26$, $p = 0.001$). In addition, mean MD, as an inverse measure of hypothalamus barrier density, was lower in females compared to males (adjusted for age, $F = 16.28$, $p < 0.001$) and higher age correlated with higher MD ($r = 0.42$, $p < 0.001$). Ongoing development of the segmentation technique will enable to automattically define the hypothalamus in all LIFE-participants (total n = 2636) and other cohort studies, to eventually reach meaningful sample sizes for genetic analyses. This might help to better understand central mechanisms of obesity.

P17 **Intermittent High-Fat Diet Intake Does Not Impair Nutrient-Induced Satiety Or Enhance Motivation For Food**

CB MASKE, DL WILLIAMS
Department of Psychology & Program in Neuroscience, Florida State University, Tallahassee, FL, United States

Binge eating is characterized by excessive food intake in a short period of time. Rodent models in which access to high-energy food is unpredictable or intermittent have been used to reproduce this phenotype. We hypothesized that elevated intake in an intermittent high-fat diet (HFD) access model could be due to impaired satiety or enhanced motivation for food. First, female rats (n=7/group) fitted with intragastric (IG) catheters received either cyclic intermittent (INT; 18 h every 5th day) or daily continuous (CONT) access to 45% HFD in addition to chow. We examined satiety responses by giving rats a 10-ml IG infusion (1 ml/min) of saline or Ensure (9.3 kcal) 15 min prior to HFD access. IG Ensure reduced 2-h HFD intake by 35% relative to IG saline in both groups, showing that INT rats are not less sensitive to nutrient load than the CONT group. Next, we assessed motivation for food in rats trained to lever press for 45-mg sucrose pellets on a progressive ratio (PR) schedule. Rats were then assigned to INT (n=6) or CONT (n=7) groups and had PR tests across 4 INT cycles. In the test after the first day of HFD exposure, both groups significantly reduced breakpoint relative to pre-HFD (47%). For the duration of the study, CONT rat breakpoints remained suppressed. INT rats had a consistent pattern of breakpoint suppression (35%) the day after HFD access, and a return to higher breakpoints after chow-only days. These results suggest that the response to both INT and CONT HFD exposure is a reduction in PR performance, at least under these training and testing conditions. We conclude that simple loss of sensitivity to IG nutrient load or elevation in motivation for food cannot explain the elevated intake observed upon intermittent access to HFD.

P18 **Knockdown Of The Monocarboxylate Transporter-2 In Nodose Ganglia Increases Food Intake And Body Weight In Rats Fed A High-Fat Diet**

N WEISSFELD, W LANGHANS, M ARNOLD
Physiology and Behavior Laboratory, ETH Zurich, Schwerzenbach, Switzerland

Peripheral, presumably enterocyte, fatty acid oxidation affects eating, but the crucial signals in this context and how the brain senses them is still unknown. Beta-hydroxybutyrate (BHB) that results from hepatic as well as intestinal fatty acid oxidation and that often inhibited eating after peripheral or central administration in laboratory animals is a viable signaling molecule. BHB may inhibit eating via vagal afferent neurons (VAN) and it enters cells via monocarboxylate transporters (MCT). We previously showed that rat VAN express MCT2, the major neuronal MCT isoform. To test whether VAN MCT2 is involved in the control of eating, we bilaterally injected an AAV-shRNA against rat MCT2 or scrambled control shRNA into the nodose ganglia of adult, male Sprague Dawley rats to knockdown VAN MCT2 mRNA expression and assessed food intake and body weight. We found that rats with a 29% MCT2 knockdown (measured 6 months after AAV-shRNA injection) i) transiently increased food intake (10%, $p < 0.05$) when switched to a high-fat diet (HFD, 60% energy from fat) 3 months after AAV-shRNA injection and ii) gained more weight (22.3%, $p < 0.05$, after

3 weeks of HFD feeding) than control animals. Our data suggest that VAN MCT2 mediates an eating-inhibitory signal that may be derived from BHB resulting from the increased intestinal fatty acid oxidation after animals are switched from chow to a HFD.

P19 **Impact Of Fat Access On Mesocorticolimbic Amylin Receptor Expression**

H NASHAWI[1], TJ GUSTAFSON[2], EG MIETLICKI-BAASE[1,2]

[1]Neuroscience Program, University at Buffalo, Buffalo, NY, United States, [2]Exercise and Nutrition Sciences, University at Buffalo, Buffalo, NY, United States

Amylin is a pancreatic- and brain-derived peptide that suppresses food intake and body weight gain and is a promising treatment candidate for obesity. Despite the fact that amylin binds throughout the CNS, including distributed sites that are known to exert control over energy balance, the expression of amylin receptor (AmR) components in these regions has not been fully characterized. Furthermore, the effect of diet on AmR expression has been largely untested. To evaluate dietary effects on CNS AmR expression, chow-maintained rats were given access to fat emulsion (1kcal/ml), or tap water as a control, 1h/day for ~1 month with no more than 2 days at a time of no fat access. Micropunched tissue samples were collected targeting the central nucleus of the amygdala (CeA), prefrontal cortex (PFC), and nucleus accumbens core (NAcC) and shell (NAcSh). We evaluated mRNA expression of AmR components (calcitonin receptors [CTR-A, CTR-B] and receptor activity modifying proteins [RAMP1, RAMP2, RAMP3]) in these sites using qPCR. Results show that all components of the AmR complex are expressed in CeA and PFC, sites that have been largely overlooked in the amylin literature, and confirm expression in NAcC and NAcSh. Fat-exposed rats showed decreased expression of some AmR components in specific nuclei; there was significantly lower expression of CTR-A in the CeA, RAMP2 in the PFC, and RAMP3 in the NAcSh in rats with fat access. No diet-related changes in AmR expression were observed in NAcC. Collectively, these findings demonstrate that chronic changes in diet can alter expression of AmR components in the mesocorticolimbic system, and also raise the intriguing question of how amylin may potentially act in CeA or PFC to control energy balance.

P20 **Differential Effects Of Fat Or Sugar On Compulsive Eating Behavior And On The Limbic System**

E ESPITIA, C ESCOBAR
UNAM, Mexico City, Mexico

Compulsive Eating Behavior (CEB) triggers anticipatory activity (AN), effort behaviors to obtain food (EB), binge eating (BE) and abstinence (AB). The digestion and absorption of sugar (S) or fat (F) is different, in spite that both are palatable food. In this study, we explored the differential effect of S or F after a first experience, after 4 weeks and after one week of abstinence, on parameters of CEB, on c-Fos activation and ΔFOSB accumulation in structures of the limbic system (LS). Rats were housed in an LD cycle with chow and water *ad-libitum*. Food intake and locomotor activity were recorded along the protocol. Access to F or S was restricted to 1 hour during 4 weeks. All the parameters of CEB were evaluated in the 4th week and during one week of abstinence AB. Brains were collected after each protocols to see the c-Fos activation and the accumulation of ΔFOSB in LS. After a first exposition BE was observed in the S group and not in the F group. S activated the prelimbic cortex (PCx); accumbens shell (AccSH) and core (AccCO) while F activated AccCO, AccSH and the insular cortex (ICx). After 4 weeks both groups showed BE; AN was developed only in the F group along the four weeks. Both groups developed EB. The S did not activate the LS, while F still activated AccCO and AccSH. In abstinence the S group did not exhibit CEB nor activation of the LS, while the F group still showed EB and activation in AccSH and ICx. We conclude that fat induces stronger signs of CEB than sugar. This project was supported by PAPIIT IN200417 and CONACyT 239403; 559045

P21 **Acute And Chronic L-Arginine Modulates Feeding In A Motivation-Dependent Manner**

K. RAPPS[1,2], N. HAZUT[1,2], L. SHBIRO[3,2], E. TANNENBAUM[1,2], S. OHEV[1,2], A. WELLER[3,2], A. SUSSWEIN[1,2]

[1]Mina and Everard Goodman Faculty of Life Sciences, Bar Ilan University, Ramat Gan, Israel, [2]Gonda Multidisciplinary Brain Research Center, Bar Ilan University, Ramat Gan, Israel, [3]Department of Psychology, Bar Ilan University, Ramat Gan, Israel

L-arginine, the dietary amino acid precursor to nitric oxide (NO), is an unconventional neurotransmitter involved in feeding control in the hypothalamus. In both the marine slug *Aplysia* and in rats, L-arginine administration inhibits feeding of animals that have a low motivation to feed, without affecting locomotion in the open field test. The current study examines the effects of L-arginine on feeding behaviour of rats with a relatively high motivation to feed. Both acute intraperitoneal administration and chronic exposure via drinking-solution were used. Acute L-arginine (150 mg/kg) increased feeding measures in both hungry and palatable-food conditions, in contrast to earlier findings in animals with low feeding motivation. In chronic oral administration, rats were given either 1% L-arginine drinking water, or regular drinking water, for three weeks. Individual feeding behaviour was tested weekly; initially in a hungry state (high motivation), followed by a satiated state (low motivation). Hungry animals in the L-arginine group had a greater motivation to feed, as demonstrated by increased feeding efficiency and appetitive behaviour. In satiated animals, chronic L-arginine reduced the drive to feed, as demonstrated by fewer meals consumed and less interest in food. Between weeks 1 and 3, L-arginine prevented the increase in eating which was seen in the control group. These experiments add further support to our hypothesis of L-arginine's modulation on feeding behavior, with differential effects dependent on feeding motivational state, evident in both acute and chronic conditions.

P22 **Investigating The Impact Of Sucrose On Sleep And Memory Function In Mice**

Y RITZE, K ADAMATZKY, CN OYANEDEL , S WENDEL, J BORN, M HALLSCHMID
University of Tuebingen, Tuebingen, Germany

Background: Sleep and metabolism have been shown to be interrelated, but the effect of specific nutrients on sleep and, in particular, its contribution to cognitive function has not been assessed. In this regard, the memory-promoting effect of sleep is of foremost interest considering that metabolic and memory impairments, especially in older age, are often associated. In this ongoing project, we are investigating the effect of a sugar-rich diet on electrophysiological sleep parameters and sleep-mediated memory function in mice. **Methods:** Male C57BL6/J mice are fed either a diet containing 30% of liquid sucrose or standard chow for eight weeks. Sleep is electroencephalographically (EEG) assessed during 24-hour periods at the beginning and after four and eight weeks. Animals perform two memory tasks at the end of the dietary intervention, the object-place and the novel-object recognition tasks. In each task, encoding is followed by a 180-min retention interval of sleep. During the recall tests, exploration of novel versus familiar object-place combinations is assessed as a measure of memory consolidation. **Results:** We will analyze sleep architecture as well as EEG power spectra, focusing on theta power during wakefulness, pre-rapid eye movement (Pre-REM) and REM sleep compared to slow wave sleep (SWS). In addition, spindle density during SWS will be assessed. Changes in sleep parameters due to the dietary intervention will be compared to respective effects on memory function. **Conclusion:** We assume that the high-sugar diet has a discernible effect on sleep architecture, particular on SWS, as well as on declarative memory formation. Experiments are intended to unravel the possible impairing effects of sugar on memory function by changes in sleep architecture.

P23 **Satiety, Energy Expenditure And Substrate Oxidation During A Controlled 48-H High Protein Vs. Medium Protein Diet, After 34 Months On Respective Diets - A Preview Respiration Chamber Study**

M DRUMMEN[1], L TISCHMANN[1], T ADAM[1], M FOGELHOLM[2], A RABEN[3], M.S. WESTERTERP-PLANTENGA[1]

[1]NUTRIM, School of Nutrition and Translational Research in Metabolism, Maastricht University, Maastricht, Netherlands, [2]Department of Food and Environmental Sciences, University of Helsinki, Helsinki, Finland, [3]Department of Nutrition, Exercise and Sports, University of Copenhagen, Copenhagen, Denmark

Effects of a high-protein (HP) vs medium protein (MP) diet on satiety, energy expenditure and substrate oxidation have been shown before. Here we assessed such effects after a 34 month low glycemic index (LGI)HP vs. medium glycemic index (MGI)MP diet, in 40 subjects of the PREVIEW-population, an EU world-wide project (EU-FP7-nr. 312057) that aims to identify the most effective lifestyle components regarding diet and physical activity in the prevention of T2D, in participants with pre-diabetes. A subgroup of 38 subjects, 21 female and 16 male (age 65 y±5.8 / BMI 29±3.9 kg/m^2) was fed with a HP: 25P/45CHO/30F or MP: 15P/55CHO/30F en% diet, in individual energy balance for 48 h in the respiratory chambers. Between the two groups no different effects on satiety or total energy expenditure were observed. The high vs. medium protein group showed a higher fat oxidation (RQ=0.82±0.02 vs. 0.84±0.02, ($p< 0.01$), a trend for a higher diet-induced thermogenesis (1.1±0.4 vs. 0.9±0.3 MJ/d; $p=0.06$), a larger positive protein balance ($p< 0.001$), a different energy balance (-0.53±0.9 vs +0.26±0.7 MJ/d; $p< 0.01$), and satiety being related to diet-induced thermogenesis ($r=0.5$; $p< 0.05$). Ad lib energy intake, as percentage of energy requirement, from a brunch afterwards did not differ between the groups. Differences in fat oxidation and energy balance were not related to the 34 month protein diets effects. Conclusion: 48-h HPLGI induced satiety was related to diet-induced thermogenesis; HPLGI vs., MPMGI resulted in a negative vs. positive energy balance, comprising differences in macronutrient balances and fat oxidation. Since differences in energy balances were not related to long-term HPLGI vs. MPMGI diets, high-protein diet effects may be supported by daily practice of this diet.

P24 **Arabinose: Acute Effects On Postprandial Glycemia**

K POL, M MARS
Wageningen University and Research, Wageningen, Netherlands

Diets that induce high changes in postprandial plasma glucose are linked to obesity and type 2 diabetes. L-arabinose and D-xylose are pentoses which may become available from dietary fiber, such as hemicellulose. These pentoses are thought to inhibit intestinal sucrase activity and therefore delay sucrose digestion and lower glycemia and insulinemia. The aim was to investigate the addition of A) L-arabinose or D-xylose to a liquid product, and of B) L-arabinose to a solid product, on glycemia and insulinemia. To this aim, 15 male subjects participated in 2 double-blind randomized cross-over tests. Test A, 3 fruit-flavored beverages of 500ml were tested: 1) 38g sucrose with 3.6g L-arabinose, 2) 38g sucrose with 3.5g D-xylose, and 3) 41g sucrose. Test B, 2 muffins of 115g containing 23g sucrose were tested: 1) 2.3g added L-arabinose, and 2) no L-arabinose addition. Plasma glucose and insulin were measured in fasting state and at fixed time points postprandial for 3 hours. Subsequent *ad libitum* food intake was measured. Peaks in glucose and insulin were significantly lower after the drink with L-arabinose and D-xylose compared to the control drink ($p< 0.01$). Glucose responses were similar after both muffins, however the insulin peak was lower for the muffin with L-arabinose ($p=0.04$). Energy intake was not different between the different types of drinks and muffins. To conclude, L-arabinose and D-xylose were potent functional ingredients to reduce glycemic and

insulin responses. The effect for L-arabinose seems more pronounced in liquids compared to more complex solid foods. Further studies should investigate the dose-response and applications in other foods.

P26 **Daily Intake Of A Polyphenol-Rich Aroniaberry Extract Elicits Changes In Plasma Glycation Adducts And Skin Glycation In Women.**

D SALTER-VENZON[1], MA MURRAY[1], K GLYNN[2], V KAZLOVA[1], J REBUHN[2], D QU[2]

[1]Nutrilite Health Institute, Buena Park, CA, United States, [2]Amway Research and Development, Ada, MI, United States

Glycation (Maillard reaction) is a series of non-enzymatic reactions that eventually form irreversibly modified compounds, Advanced Glycation End Products (AGEs). AGE accumulation elicits glyco-oxidation and is linked to inflammation, metabolic dysfunction, a chronic disease. Dietary and lifestyle modifications to reduce AGE accumulation are warranted. *Aronia melanocarpa L* (chokeberry) contains antioxidative phytochemicals that may exhibit normoglycemic properties via non-specific activation of PPARg. Here, we performed an explorative pilot study in which we hypothesized a daily serving of standardized Aronia extract might affect glycation. 107 healthy females, ages 30-65, BMI 27-35, and with skin glycation values above the mean-for-age skin autofluorescence value (SAF) were recruited. Subjects were randomly assigned into one of three treatments; 1) 200mg aronia (high-polyphenol;HPA), 2)130mg aronia/122mg licorice root (low polphenol;LPA), 3) Placebo (P). Asessment of skin glycation was via AGE Reader device SAF and plasma glycation adducts via liquid chromatography-tandem mass spectrometry (LC-MS/MS) at baseline, and after 8 and 16 weeks. The within-group comparison SAF change over 16 weeks was -0.136+/-0.061AU (p=0.035), -0.061+/-0.062AU (p=0.341), -0.053+/-0.058AU (p=0.366) for HPA, LP, and P, respectively. We observed the most pronounced effect between week 8 and 16; median HPA-SAF decreasing -0.181AU and P-SAF increasing 0.048AU (paired t-test, p=0.073). A positive correlation was seen between SAF and plasma methylgloxyl (r=0.4, p< 0.0001) and pentosidine (r=0.3, p=0.0013). Results suggest glycation values can be meaningfully changed by a short-term dietary modification. Additional studies with larger study populations may be warranted.

P27 **Neurobehavioral And Environmental Constructs Are Associated With Diet Quality During Pregnancy**

TR NANSEL[1], LM LIPSKY[1], MS FAITH[2], A LIU[1], N SANJEEVI[1], AM SIEGA-RIZ[3]

[1]Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD, United States, [2]University of Buffalo SUNY, Buffalo, NY, United States, [3]University of Virginia, Charlottesville, VA, United States

Research indicates that neurobehavioral factors, including food reward sensitivity and self-control, in conjunction with the food environment, may influence dietary behaviors. However, these constructs have not been examined in pregnancy, a time of changing appetite and eating behaviors, and when dietary intake has implications for maternal and child health outcomes. This study examined associations of food reward sensitivity, self-control, and the home food environment with pregnancy diet quality. Women were recruited at ≤12 weeks gestation and completed the Modified Yale Food Addiction Scale (MYFAS) assessing addictive-like eating; the Power of Food Scale (PFS) measuring hedonic hunger, the Delay of Gratification Inventory food subscale (DGI), the Barratt Impulsivity Scale (BIS), and the Home Food Inventory (HFI) yielding an obesogenic food score. Participants completed 24-hour dietary recalls each trimester, from which the Healthy Eating Index 2015 (HEI, range 0-100), a measure of conformance to US dietary guidelines, was calculated across pregnancy. Separate linear regression models controlling for age, marital status, education, household size, and income examined associations of each construct with HEI. The sample (n=364) had a mean BMI of 26.57±6.42 and mean HEI of 54.27±13.46. Women with a BMI ≥30 had a significantly lower mean HEI (48.95±13.49) than those with a BMI of 18.5-24.9 (56.86±13.32) or 25-29.9 (53.78±12.69) (p< .001). HEI was associated inversely with PFS (b=-2.76±1.12, p=.01), MYFAS (b=-2.68±1.12, p=.01), and HFI (b=-0.23±0.10, p=.02), and positively with DGI (b=0.61±0.20, p=.002), but was unassociated with BIS. Findings suggest the relevance of neurobehavioral and environmental constructs in understanding eating behaviors of women during pregnancy.

P28 **Within-Subject Weight Variability In Infants Prospectively Predicts Increases In Zbmi**

MR LOWE, L BENSON, F ZHANG
Drexel University, Philadelphia, PA, United States

Weight variability (WV) is measured by collecting repeated within-subject weights over weeks or months and calculating the average distance between each weight and each individual's best-fitting regression line (i.e., the root mean square error or RMSE). Our lab has previously published 3 papers showing that RMSE predicts future weight gain, brain activation patterns to milkshake tastes and poorer weight loss maintenance. Further, those with increased WV are more likely to have a family history of overweight. The current study extends these findings to over 1,000 infants who are part of a large prospective data set (the Avon Longitudinal Study of Parents and Children). Controlling for z-BMI gain in year 1, RMSE scores based on 4 z-BMI measurements during year 1 predicted greater z-BMI gain in year 2. Similarly, RMSE based on 3 z-BMI measurements in year 2 predicted greater z-BMI gain in year 3. Because RMSE and weight gain during the same year were themselves significantly correlated, we ran regression analyses showing that both measures independently predicted subsequent 1-year weight gain. Thus weight variability, independently of co-occurring z-BMI increases, predicts subsequent gains in z-BMI. These findings extend our previous results with adolescents and adults to infants. We

speculatively propose that greater WV reflects a decreased sensitivity of homeostatic mechanisms that normally keep body weight highly stable. The same decreased sensitivity could make those higher in WV more susceptible to future weight gain.

P29 **Exendin-4 Conjugated To Vitamin B12 Improves Glucose Tolerance In Mice And Shrews Without Inducing Vomiting Or Hypophagia**

T BORNER[1], E SHAULSON[1], LM STEIN[2], JL WORKINGER[3], RB JAIME-LARA[1], CG LIBERINI[2], RP DOYLE[3,4], MR HAYES[1,2], BC DE JONGHE[1]

[1]Department of Biobehavioral Health Sciences, School of Nursing, University of Pennsylvania, Philadelphia, PA, United States, [2]Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States, [3]Department of Chemistry, Syracuse University, Syracuse, NY, United States, [4]Department of Medicine, Upstate Medical University, State University of New York, Syracuse, NY, United States

Glucagon-like peptide-1 receptor (GLP-1R) agonists which are FDA-approved for treating type 2 diabetes mellitus (T2DM), often produce multiple undesired side effects such as nausea and vomiting and, in approx. 20% of T2DM patients, undesired anorexia. Our group developed a conjugate of vitamin B12 bound to the GLP-1R agonist exendin-4 (Ex4), which displays enhanced proteolytic stability and reduced brain penetrance. Thus, we evaluated the efficacy of the conjugate (B12-Ex4) to improve glucose tolerance without inducing anorexia (in mice and shrews) and vomiting (in shews). Since the mouse model is a non-vomiting species, we chose to utilize the musk shrew (*Suncus murinus*) to test B12-Ex4 on glycemic profile due to its comparable physiology to humans for inducing emesis. In both mice and shrews, acute administration of native Ex4 (mice: 1 nmol/kg, shrews: 5 nmol/kg significantly suppressed 24h food intake; in contrast equimolar administration of B12-Ex4 in either species had no effect on feeding. In both species, native Ex4 and B12-Ex4 were able to equivalently blunt the rise in blood glucose levels following IP glucose bolus administration. Importantly, the emetic response observed in shrews following native Ex4 administration was markedly attenuated in B12-Ex4 treated animals (87.5% vs. 12.5%, n=8/group, $p< 0.05$). In addition, the total number of emetic episodes occurring within 90-min post treatment was significantly reduced in B12-Ex4 compared to Ex4 (0.12±0.12 vs. 2.12±0.61, n=8/group, $p< 0.05$). Collectively, these findings highlight the potential therapeutic value of B12-Ex4 as a novel treatment for T2DM, especially in a non-obese population, with reduced adverse effects but similar hypoglycemic potency to native Ex4.

P30 **Provision Of A To-Go Container Attenuates The Portion Size Effect In Women**

FM ZURAIKAT, LS ROE, AD SMETHERS, BJ ROLLS
The Pennsylvania State University, University Park, PA, United States

Serving larger portions leads to increased food and energy intake; however, little is known about strategies to moderate this response. This study tested how providing a container to take home uneaten food influenced the effect of portion size on intake at a meal. Women were randomly assigned to 1 of 2 subject groups: a To-Go Group (n=27) that was informed prior to each meal that their uneaten food would be packaged to take home after the meal and a Control Group (n=26) that was not given their uneaten food to take home. In a crossover design, subjects came to the lab once a week for 4 weeks to eat a dinner of 5 foods. Across meals, the portion size of all foods was varied (100%, 125%, 150%, and 175% of baseline). Results showed that the portion size effect, defined as the trajectory of intake across the weight of food served, differed significantly by subject group ($P=0.025$). In the Control Group, increasing the portion size of all foods led to substantial increases in the weight and energy consumed ($P< 0.0001$). Women in the Control Group consumed an additional 64 g of food and 90 kcal for every 100 g served beyond baseline until intake leveled off. In contrast, food and energy intake of women in the To-Go Group increased by only 17 g and 19 kcal for every additional 100 g served; these increases did not differ significantly from zero ($P>0.15$). Thus, the effect of portion size on intake was attenuated in the To-Go Group compared to the Control Group. These data show that providing an opportunity to take home uneaten food can be an effective strategy to reduce overconsumption from large portions at a meal.

P31 **Psychobehavioral Variables And Their Impact On Insulin Resistance During Lifestyle Intervention &Ndash; A Preview Study**

TC ADAM[1], M DRUMMEN[1], AJ MARTINEZ[2], S NAVAS-CARRETERO[2], T HANDJIEVA-DARLENSKA[3], S POPPITT[4], M PAULINO[4], G STRATTON[5], I MACDONALD[6], E SIMPSON[6], J BRAND-MILLER[7], E JALO[8], M FOGELHOLM[8], T MEINERT-LARSEN[9], A RABEN[9], MS WESTERTERP-PLANTENGA[1]

[1]Maastricht University, Department of Human Biology, Maastricht, Netherlands, [2]University of Navarra, Department of Nutrition and Physiology, CIBER Fisiopatología Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III, Navarra, Spain, [3]Medical University of Sofia, Department of Pharmacology and Toxicology, Sofia, Bulgaria, [4]University of Auckland, Human Nutrition Unit, School of Biological Sciences, Auckland, New Zealand, [5]Research Centre in Applied Sports, Technology, Exercise and Medicine (A-STEM), Swansea, United Kingdom, [6]University of Nottingham

Medical School, School of Biomedical Sciences, Nottingham, United Kingdom, [7]University of Sydney, Charles Perkins Centre and School of Life and Environmental Biosciences, Sydney, Australia, [8]University of Helsinki, Obesity Research Unit, Research Program Unit, Diabetes and Obesity, Helsinki, Finland, [9]Department of Nutrition, Exercise and Sports, Kopenhagen, Denmark

Psychobehavioral variables have been associated with insulin resistance and obesity, and may interfere with weight loss maintenance through neuroendocrine and inflammatory pathways. Long-term studies are warranted to gauge their role for treatment efficiency. The PREVIEW study was initiated to identify most effective lifestyle components regarding diet and physical activity in the prevention of T2D in participants with impaired glucose tolerance, comprising an 8-week weight loss period followed by a three-year intervention period. Weight, HOMA-IR, C reactive protein (CRP, mg/dl), stress, mood, and eating behavior (PSS, POMS, TFEQ, resp.) were assessed in 2166 (m/f:698/1468) overweight (BMI ≥ 25kg/m^2) participants (age:25-70) at baseline, 8, 28, and 56 weeks. From baseline to 56 weeks HOMA-IR (3.7±2.4; 1.9±1.5), PSS (14.07±6.3; 13.9±6.6), and CRP (5.3±7; 2.8±5) consistently decreased (all $p< 0.05$), dietary restraint (7.98±4.1; 13.15±3.8) and vigor (15.8±5.5; 17.5±5.7) increased (all $p< 0.05$). Mixed modelling estimates showed baseline cognitive restraint, and vigor to be associated negatively with HOMA-IR, hunger positively (all coefficients $p< 0.05$). Perceived stress, hunger, tension, fatigue, and mood disturbance were associated positively with HOMA-IR at 28 weeks, vigor negatively (all coefficients $p< 0.05$), corrected for fat mass, BMI, age, gender, protein intake (g/kg), and physical activity (counts/minute). Linear regression showed a significant association between changes in HOMA-IR and changes in tension, depression, and anger only for the first four-month of the intervention period (R^2=0.10;$p< 0.05$). The results suggest that psychobehavioral parameters may be especially relevant for metabolic health outcomes in early stages of weight maintenance.

P32 **Does Exposure To Weight Control Cues Lead To Reduced Food Intake? A Systematic Review With A Meta-Analysis**

NJ BUCKLAND[1], V ER[2], I REDPATH[3], K BEAULIEU[4]

[1]Department of Psychology, University of Sheffield, Sheffield, United Kingdom, [2]Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, United Kingdom, [3]The Behaviouralist Ltd. , London, United Kingdom, [4]Appetite Control and Energy Balance Group, School of Psychology, University of Leeds, , Leeds, United Kingdom

A number of studies suggest that exposure to cues associated with weight control (e.g. weighing scales, low calorie foods) can prompt controlled food intake in tempting food environments. However, findings are mixed. This systematic review and meta-analysis aimed to evaluate the effect of weight control cues on food intake and examine: (i) whether such effects are stronger in individuals with strong compared to weak weight control goals and; (ii) whether certain types of cues are more effective than others. Four electronic databases were searched for articles published up to January 2017. Hedge's g was used to calculate effect sizes based on mean food intake, standard deviations and sample sizes extracted from relevant publications and, a random effects model was used for the meta-analysis. Twenty-four articles consisting of 25 studies were eligible. Data from 24 studies (30 effect sizes) were available for the meta-analysis. Overall, weight control cues reduced food intake, to a trivial effect (ES: -0.139, 95% CI: -0.264 to -0.014). When studies which induced negative affect were removed, a small-to-moderate effect showed that weight control cues reduced food intake in individuals with strong weight control goals (ES: -0.446, 95% CI: -0.789 to -0.103) but, this effect was trivial and non-significant for individuals with weak weight control goals (ES: 0.075, 95% CI: -0.149 to 0.299). Cue type and level of engagement did not significantly moderate the effect; however, specific cues (low calorie foods and thin models) and attended engagement yielded significant effects. In conclusion, weight control cues reduce food intake in individuals with strong weight control goals. Funded by Cancer Research UK; PROSPERO registry#CRD42016052396.

P33 **Smaller Portions Of An Energy-Dense EntréE Incentivize The Consumption Of Vegetables In Children Ages 7-9 Years**

A ORLOSKI[1], JM BRUNSTROM[2,3], JO FISHER[1]

[1]Department of Public Health, Center for Obesity Research and Education, Temple University, Philadelphia, PA, United States, [2]National Institute for Health Research, Bristol Biomedical Research Centre, University Hospitals Bristol NHS Foundation Trust and University of Bristol, Bristol, United Kingdom, [3]School of Experimental Psychology, University of Bristol, Bristol, United Kingdom

Offering children large portions of energy-dense entrées promotes intake of those foods and may reduce the consumption of other foods that accompany a meal. Accordingly, we hypothesized that offering smaller portions of an energy-dense entrée might increase the incentive for children to consume vegetables in a meal. In a between-subjects design, children (*N*= 102, range 7-9 years) were offered an entrée portion size that accounted for either 50%, 75% or 100% of their optimal intake (147 g, 220 g, 293 g, respectively). In a control condition, each child was also offered a portion that provided 125% of their optimal energy intake at dinner. Fixed amounts of peas (85.0 g) and corn (85.0 g) were provided in each meal and total energy intake was assessed using weighed food-intake methods, in conjunction with manufacturers' nutritional information. Children assigned to the 50% and 75% energy condition consumed less total energy at the meal, compared to the children in the 100% condition (343.1 kcal and 391.5 kcal vs 521.2 kcal, respectively; $p< 0.0001$). Children in the 50% and 75% condition also consumed a greater proportion of energy from vegetables compared to the

control condition (125%), $p < 0.01$. Results from this study indicate that offering children smaller portions of energy-dense entrées may be helpful in promoting the consumption of energy derived from vegetables.

P34 **Treatment Experiences Of Women With Binge Eating Disorder (Bed): A Qualitative Study Of Methylphenidate (Mp) Vs Cognitive Behavioral Therapy (Cbt)**

E MOGHIMI[1, 2], C DAVIS[1,2], R BONDER[1], Y KNYAHNYTSKA[2], L QUILTY [2]

[1]York University, Toronto, ON, Canada, [2]Centre for Addiction and Mental Health, Toronto, ON, Canada

The following qualitative study enrolled 15 treatment completers (8 MP, 7 CBT) from a previous randomized controlled trial of MP therapy vs CBT in women with BED and a BMI ≥25, in order to understand their lived experiences with the therapeutic process, and how it impacted their binge episodes and weight management. Semi-structured interviews were used to obtain their narrative accounts; key themes were then identified from transcribed tape recordings, using thematic analysis. According to patients, the success of both therapies was defined as reduced binge episodes, not weight loss. In MP treatment, the primary benefit was viewed as its ability to reduce the preoccupation with food, and hence, binge frequency. In addition, a positive patient-physician relationship was reported to be integral to treatment success. In CBT, though the beneficial effects were not immediate, patients had a strong focus on the long-term binge management skills they learned in therapy. In both treatments, stress was commonly described as a reason to binge and/or relapse. Therefore, it is proposed that both treatments should have a stronger focus on adaptive methods of coping with stress. These qualitative findings add a much needed perspective on clinical treatments for compulsive overeating, especially considering that a psychomotor stimulant similar to MP is the only approved pharmacotherapy for BED – and to date, little is known about the patient's subjective experiences.

P35 **Influence Of Holistic And Analytic Information Processing Styles On The Dishware Size Effect**

A.Y. SIM, B.K. CHEON

Clinical Nutrition Research Centre (CNRC), Singapore Institute for Clinical Sciences (SICS), Agency for Science, Technology and Research (A*STAR) and National University Health System, Singapore, Singapore

Prior studies have suggested that individuals, as well as cultures, may vary in the extent to which they engage in holistic and analytic information processing styles. Holistic cognition involves the processing of information in an interdependent and context-sensitive manner, while analytic cognition involves processing information as discrete elements and independent from its context. We examined whether these basic perceptual/cognitive orientations may influence a well-studied eating behaviour phenomenon, the dishware size effect, in which the amount of food consumed may be influenced by the size of the dishware (i.e. larger plates resulting in larger portion of food consumed). We demonstrated that participants ($n = 115$, women = 71) self-served and consumed more food (ad-libitum access to a local fried rice dish) when using and eating from a larger plate (LP; served 291 ± 228 kcal and consumed 290 ± 229 kcal) compared with a smaller plate (SP; served 211 ± 109 kcal and consumed 203 ± 100 kcal) ($p \leq 0.01$). Importantly, participants who endorsed greater levels of holistic thinking on the Analysis-Holism Scale, especially the subscales of Attitude towards contradiction and Locus of attention, served and consumed lesser food in LP ($r \geq 0.27$, $p \leq 0.03$) and consequently exhibited smaller variations in portions of food self-served and consumed based on the size of dishware used (LP vs. SP) ($r \geq 0.40$, $p \leq 0.03$). Findings suggest that the susceptibility of individuals to the dishware size effect may be associated with an individual's dispositional tendency to process information in a holistic (vs. analytic) manner.

P36 **Associations Between Parental Control And Children&Rsquo;S Eating Behaviors In A Quick-Service Restaurant**

S TAURIELLO, J BOWKER, S ANZMAN-FRASCA

University at Buffalo, Buffalo, NY, United States

One third of children consume a quick-service restaurant (QSR) meal on any given day; such meals have been linked to increased daily energy intake and poor diet quality. Although largely unstudied in QSR, some findings suggest greater parental control in the home predicts healthier child eating behaviors. This study aimed to examine the associations between parental control and children's meal selection and intake within a QSR. Families with 4-to-8-year-old children were recruited from one location of a regional QSR chain, and randomly assigned to return to the restaurant during an intervention or control period for a broader pilot intervention study. Researchers recorded children's orders and collected leftovers for quantifying dietary intake via weighed plate waste. Parental control was assessed by parent-report questionnaire and operationalized as who chose the child's meal, with the parent choosing alone indicating greater control. General linear models were used to examine parental control as a predictor of total calories and saturated fat ordered and consumed (N=54 families). Parental control predicted fewer total calories ordered for children (M=766.90) compared to no parental control (M=866.60) at a trend level (p=.07). Parental control did not predict child total saturated fat ordered or child intake. Results did not change when controlling for study group. Parental control may reduce the caloric content of selected children's meals in QSR. However, more research is needed given the absence of relationships with child intake and the pilot nature of the present study.

P37 **Attributions For Food Intake: Attributional Patterns And Motivational Processes**

S SPANOS
University of New South Wales, sydney, Australia

Food intake can be strongly influenced by external factors. When explaining why they ate as much as they did, people typically fail to acknowledge the impact of external factors (such as portion size), instead attributing their behaviour to internal factors (such as hunger). This attributional pattern seems comparable to attributions people make for their behaviour more generally. Two studies were conducted to examine potential self-serving attributional patterns for food intake. In Study 1, participants (N = 184) read hypothetical scenarios about their eating behaviour and made attributions for the outcome. Participants were more likely to attribute positively framed eating behaviour ("success") in terms of internal rather than external factors, whereas negatively framed eating behaviour ("failure") was explained in terms of external rather than internal factors. In Study 2, participants (N = 103) received positive or negative feedback about their food intake and made attributions for their eating outcome. Positive eating outcomes resulted in greater attributions to self-restriction and self-control compared to negative eating outcomes. Exploring how people conceptualise their food intake, as well as the motivations that underlie these processes, can provide a greater understanding of how self-evaluations impact health and wellbeing.

P38 **Are Children Aged 8-11 Capable To Understand And To Apply The Energy Density (Ed) Concept In Theory? Results Of A Serious Game Addressing The Energy Density Concept**

I MACK [1], N REIBAND[1,2], S EICHHORN[1], C BAYER[1], N SCHäFFELER[1], S ZIPFEL[1]
[1]Department of Psychosomatic Medicine and Psychotherapy, Tuebingen, Germany, [2]Department of School Psychology, Tuebingen, Germany

Introduction: Both the portion size and energy density (ED) of foods have large effects on energy intake, and contribute to the obesity epidemic. Nutritional education for children is generally based on the food-pyramid concept and the "5 (fruit and vegetable) a day" approach. The ED concept is applied successfully in the nutritional education of adults but for children it is not clear how well they can understand and apply it. Methods: A motion-controlled serious game for children addressing all the three core areas of nutrition, physical activity, and psychosocial factors has been developed (KOP-Kids Obesity Prevention Program). It is the first serious game, which extensively targets the ED concept in the nutrition section. The children analyze various foods in the different food groups with regards to their contents of fat, carbohydrates, protein, fiber and water. In the next step, the children have to apply their knowledge in two different tasks. These tasks allow us to measure not only whether the children have understood the ED concept but also whether they can apply it to unknown foods under time pressure where for food pairs the food with the lower energy density has to be selected. Results: Eighty-three school (age: 9.7±0.5 years, BMI z-score: 0.1±1.2) played the game. Under time pressure the children were able to classify unknown foods equally as the known foods according to their ED (hit rate: 72.3±14.9% vs. 70.2±14.3%, p=.232). However, it took the children longer to make a decision when unknown foods in comparison to known foods were presented (1537±347ms vs. 1489±456 ms, p< .001). Discussion: Primary school children do understand the ED concept and the latter could be applied in standard nutritional education for children.

Thursday, July 19, 2018

8:30 - 10:30 AM	Calusa ABC
NITA Symposium	

Chair(s): Ruth Harris

8:30 **Hunger Inhibits Pain Responses Through A Hypothalamic-Hindbrain Peptidergic Circuit**

AL ALHADEFF, E HERNANDEZ, JN BETLEY
University of Pennsylvania, Philadelphia, PA, United States

Hunger elicits a variety of physiological changes to facilitate food seeking and consumption. How these changes affect the perception of environmental stimuli is not fully known. Here, we discovered that hunger attenuates the behavioral response to and the negative affect associated with long term, inflammatory pain without altering acute nociceptive responses. Optogenetic activation of hypothalamic Agouti-Related Protein (AgRP)-expressing neurons specifically abrogated inflammatory pain responses, providing a neural substrate for the interaction between hunger and pain. Systematic functional analysis of each major AgRP projection subpopulation revealed that the neural processing of hunger and pain converge in the hindbrain parabrachial nucleus (PBN). Strikingly, activity in AgRP-PBN neurons blocks the response to inflammatory pain as effectively as hunger or analgesics. Furthermore, activating the ~300 AgRP neurons that project to the PBN during an ongoing pain response is sufficient to mediate a behavioral switch and suppress nocifensive behavior. This suppression of inflammatory pain by hunger is driven by NPY signaling, as PBN NPY Y1 receptor antagonism blocked the effects of hunger or AgRP-PBN neuron stimulation on pain. This effect is not likely mediated by post-synaptic PBN CGRP neurons – which are involved in food intake and affective threat memory – because Fos expression in these neurons is low following inflammatory pain. Current experiments are determining the PBN neuron population(s) that transmit inflammatory pain, and emerging evidence highlights a subpopulation of glutamatergic neurons. Taken together, these experiments reveal that hunger suppresses the perception and response to inflammatory pain through a hypothalamic-hindbrain peptidergic circuit.

8:45 **A Locus Coeruleus To Lateral Hypothalamus Circuit For Suppression Of Feeding**

NR SCIOLINO[1], N PLUMMER[1], J AMIN[1], CA MCGEE[1], AV KRAVITZ[2], MR BRUCHAS[3], P JENSEN[1]
[1]NIH-NIEHS, RTP, NC, United States, [2]NIH-NIDDK, Bethesda, MD, United States, [3]Washington University, St. Louis, MO, United States

Altered norepinephrine (NE) signaling is implicated in overeating and excessive weight gain in humans. Although modulators of NE are currently used for weight loss, they result in adverse side-effects due to their broad actions throughout the nervous system, highlighting the need to identify specific NE circuits that suppress feeding without other effects. Towards this goal, we used chemogenetics to reveal that activation of NE-locus coeruleus (LC) neurons results in suppressed feeding and weight loss. This key finding, along with evidence that feeding is suppressed by NE agonists delivered directly in the lateral hypothalamus (LHA), suggests that increased NE-LC activity suppresses feeding via LHA inputs. To test this, we expressed a cre-dependent ChR2 or eYFP control in the LC of dopamine beta-hydroxylase cre mice (*Dbh*^{cre}). We found photostimulation of the LC-LHA circuit suppressed feeding in ChR2 mice relative to controls**.** Interestingly, photostimulation had no effect on anxiety-like behavior in the elevated plus maze, demonstrating the LC-LHA circuit regulates feeding independent of anxiety. To ascertain if NE signaling is required by LC neurons to suppress feeding, mice with disrupted NE synthesis in LC neurons (LC-Dbh mutants) and littermate controls were injected i.p. with vehicle or the alpha-2 adrenoceptor antagonist yohimbine, which is well-known to evoke NE release. We found yohimbine suppressed feeding in littermate mice, yet had no effect in LC-Dbh mutants, indicating that NE is required for suppression of feeding. Collectively, these findings reveal a novel role for NE signaling in the LC-LHA circuit for suppression of feeding. Our findings suggest targeting specific NE neural pathways may yield improved weight loss therapies without anxiety side-effects.

9:00 **Disrupted Instrumental Reinforcer Devaluation In Binge Eating Prone Rats**

JV LEMON[1], CL SISK[1,2], KL KLUMP[1], AW JOHNSON[1,2]
[1]Michigan State University, Department of Psychology, East Lansing, MI, United States, [2]Michigan State University, Neuroscience Program, East

Lansing, MI, United States

Binge eating (BE) is characterized by the consumption of a large amount of palatable food (PF) in a short period of time and is a core feature of all major sub-types of eating disorders (EDs). Individuals with EDs display abnormal behavioral regulation, including behavioral rigidity and high impulsivity. The reinforcer devaluation task can be used to examine decision-making following reductions in the value of a food reinforcer—deficits in this form of flexible goal-directed behavior could contribute to abnormal behavioral regulation seen in EDs. In the current study, female rats were trained to respond on two levers for the delivery of two food reinforcers (sucrose and maltodextrin solutions). At the test stage, rats were provided 1hr access to one of the two reinforcers to allow for devaluation via sensory specific satiety, immediately followed by an extinction test with both levers. Normal rats typically reduce responding on the lever associated with the devalued reinforcer (i.e., intact goal-directed responding). Subsequently, we used intermittent access to PF (i.e., Betty Crocker Extra Creamy Vanilla Frosting) to identify high (BE prone [BEP]; n=14), intermediate (BE neutral [BEN]; n=48), and low (BE resistant [BER]; n=13) phenotypes of BE. Prior reinforcer devaluation performance showed BEN and BER rats suppressed responding on the lever associated with the devalued reinforcer while BEP rats did not. This deficit in BEP rats did not reflect an insensitivity to sensory-specific satiety as during a food choice test, BEP rats consumed significantly more of the non-devalued and less of the devalued reinforcer than BER and BEN rats. These findings suggest deficits in goal-directed behavior may contribute to the aberrant behavioral regulation seen with EDs.

9:15 **Preproglucagon Neurons Are Sufficient For Physiological Satiety In Lean Mice, But Are Only Necessary Under Selective Conditions**

DI BRIERLEY[1], F REIMANN[2], FM GRIBBLE[2], S TRAPP[1]

[1]Department of Neuroscience, Physiology and Pharmacology University College London, London, United Kingdom, [2]Metabolic Research Laboratories University of Cambridge, Cambridge, United Kingdom

GLP-1-producing hindbrain preproglucagon (PPG) neurons are sufficient to reduce food intake, however whether this is due to potentiation of physiological satiety, or induction of nausea, is unclear. Furthermore, the conditions under which they are necessary for satiety remain to be determined. To address this, transgenic mice expressing Cre recombinase in PPG neurons were stereotaxically injected with Cre-dependent AAVs encoding either hM3Dq or hM4Di DREADD receptors. Cohorts (n=8) were used to investigate the effects of CNO-induced activation (PPG-Gq) or inhibition (PPG-Gi) of PPG neurons on feeding behaviour under free-feeding, fasted and Ensure pre-load conditions using within-subjects designs. Food intake was recorded using automated pellet dispensers with concurrent video recording for coding of behavioural satiety sequences (BSS). In free-feeding PPG-Gq mice, CNO elicited a robust sex-independent anorectic effect, driven by reduced intake during hours 1-5, with no compensatory refeeding observed within 48hrs. Intake was also supressed in these mice following an 18hr fast. Under these conditions, CNO advanced the onset of satiety from 15-20mins to within 5mins from the start of the BSS test, with the typical post-prandial behavioural sequence essentially maintained. In PPG-Gi mice, CNO did not elicit a hyperphagic response in free-feeding or 18hr fasted mice. However, following a 15min Ensure preload, chow intake was increased during hour 1, driven by a reduced latency to meal 1. With 1hr Ensure access, liquid diet intake itself was increased by CNO, followed by a modest compensatory decrease in chow intake during the next hour. Thus, while PPG neurons are seemingly sufficient to induce physiological satiety, they may only be necessary following high-volume meals.

9:30 **Ventral Tegmental Area And Nucleus Tractus Solitarius Oxytocin Receptor Activation Reduces Motivational Aspects Of Feeding**

HS WALD[1], ZY ONG[2], A CHANDRA[1], HJ GRILL[1]

[1]University of Pennsylvania, Philadelphia, PA, United States, [2]University of New South Wales, Sydney, Australia

Oxytocin (OT) is a neuropeptide produced in paraventricular hypothalamic neurons whose CNS receptor-mediated actions include feeding inhibition. OT is being evaluated as a potential obesity treatment, yet the contribution of OT receptors (OT-R) to appetitive and motivational aspects of feeding is unknown. We administered central (lateral ventricle; 1ug/ul)) OT and observed reductions in fixed ratio (FR)5 and progressive ratio (PR) responding for sucrose as well as for reinstatement of chocolate-seeking. As OT-Rs are expressed throughout the brain, we investigated whether OT-R activation in specific brain nuclei reduces motivational aspects of feeding. Combining retrograde tracers and OT immunohistochemistry, we focused attention on three OT-R expressing nuclei [ventral tegmental area (VTA), nucleus accumbens core (NAcC), and nucleus tractus solitarius (NTS)] that were then assessed functionally. OT administration to the VTA (0.25 and 1ug/nl) reduced FR5 responding and in the NTS reduced FR5 and PR responding for sucrose, supporting a role for NTS and VTA OT-R signaling in food motivation. In contrast, OT delivery to the NAcC did not affect FR5 or PR responding. Together, the data indicate that central OT-R activation reduces motivational aspects of feeding and that these effects are conveyed, in part, by engaging OT-R in the NTS and VTA. Complementary ongoing experiments are using antagonist pharmacology and shRNA OT-R knockdown to evaluate effects of reducing NTS and VTA OT-R signaling on food motivation. Supported by DK-21397

9:45 **The Effects Of Sweetness And Carbohydrate Content On Diet-Induced Thermogenesis And Gastric Emptying**

G CAMPS[1], MG VELDHUIZEN[2,3], DM SMALL[3], C DE GRAAF[1], PAM SMEETS[1,4]

[1]Human Nutrition, Wageningen University, Wageningen, Netherlands, [2]John B Pierce Laboratory, New Haven, CT, United States, [3]Department of Psychiatry, Yale University, New Haven, CT, United States, [4]Image Sciences Institute, UMCU, Utrecht, Netherlands

Recent work has shown that taste can influence carbohydrate metabolism. In particular, the sweetness of a beverage influences dietary induced thermogenesis (DIT). One component of the underlying physiological mechanism could be gastric emptying (GE). This study sought to measure the effect of sweetness and carbohydrate content on dietary induced thermogenesis and gastric emptying. 15 healthy participants (80% female; age 21±1.82 y; BMI 22.95±1.85 kg/m^2) enrolled in a randomized 2x2 cross-over study in which sweetness (LS/HS) and energy load (LE/HE) of a uniquely flavored 355-ml drink were varied. In 4 sessions, energy expenditure (EE) was assessed with a ventilated hood for 20 min pre-ingestion and 50 min post-ingestion (ΔEE defined as DIT. In another 4 sessions, GE was determined by MRI measurements of the stomach before and after ingestion at t=0, 15, 20, and 35 min. Higher energy loads increased DIT more (main effect energy load, ϱ< .001). In the HE load condition a significant effect of sweetness was observed such that the mismatched LS/HE beverage induced a higher DIT than the matched HS/HE beverage (ϱ< .05). Higher energy loads increased GE half-time (t50) more (main effect energy load, ϱ< .001). In the HE load condition a significant effect of sweetness (ϱ< .05) was observed in which the mismatched LS/HE beverage induced a lower t50 than the matched HS/HE. The combination of EE and GE results implies that under the HE condition sweetness delays GE. This prevents intragastric nutrients from being immediately metabolized thereby explaining the observed lower DIT. In conclusion, our results confirm that sweetness can influence metabolism and suggest that this is mediated by gastric emptying.

10:00 **Patients Who Prefer &Ldquo;Sweet&Rdquo; Lose More Weight Following Roux-En-Y Gastric Bypass But Not Following Vertical Sleeve Gastrectomy.**

KR SMITH[1], TH MORAN[1], S CARNELL[1], KE STEELE[2]

[1]Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, United States, [2]Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD, United States

Roux-en-Y gastric bypass (RYGB) and vertical sleeve gastrectomy (VSG) are the two most common bariatric procedures for significant and sustained weight loss in individuals with obesity. To understand how these bariatric procedures affect hedonic control of appetite, patients undergoing RYGB (N=16) or VSG (N=12) were asked their pre-surgical preference for ice cream or french fries and then given a taste preference test prior to and 2 weeks, 3 months, and 6 months post-surgery. Twelve tastants of varying sugar (0%, 10%, 20%) and fat content (0%, 3.4%, 10%, 33%) were presented in randomized order to each patient. Patients were instructed to taste, rate (on a visual analog scale), and expectorate each tastant, then rinse with water between stimulus presentations. These preferences and ratings were then correlated with observed weight loss. Among patients who underwent RYGB, those who gave higher ratings to tastants with added sugar lost more weight than those who gave lower ratings. This was particularly true for pre-surgical ratings of the 10% fat and 10% added sugar mixture, which predicted weight loss at 3 and 6 months after surgery. This correlation did not hold for VSG recipients. Furthermore, whereas all patients regardless of bariatric intervention lost a significant amount of weight from baseline, those receiving RYGB who selected “sweet” (ice cream) over “salty” (french fries) prior to surgery lost the most weight. These preliminary data suggest that patients who present with high preferences for sugar prior to surgery may be better suited for RYGB rather than VSG to achieve optimal weight loss success.

10:15 **The Impact Of Elevated Body Mass On Neural Responses During Appetitive Prediction Error**

GE SHEARRER[1], TR NANSEL[2], LS LIPSKY[2], JR SADLER[1], KS BURGER[1]

[1]University of North Carolina, Chapel Hill, NC, United States, [2]National Institutes of Health Child and Human Development , Bethesda, MD, United States

Preclinical and human neuroimaging research shows repeated exposure to highly palatable foods and/or elevated weight promotes an insensitivity to punishment in striatal regions. Despite being well characterized in animal models, very little is known about these processes in humans. We hypothesized that women with an elevated BMI would show greater striatal response to a sub-palatable taste (i.e., punishment) during negative prediction error. Women (n=47; BMI= 25.5±5.1) were ‘trained’ to associate specific cues paired to either a: highly palatable milkshake, or a sub-palatable milkshake. We then violated these cue-taste pairings in 40% of the trials showing a palatable cue followed by the sub-palatable taste (negative prediction error). Analyses were corrected for multiple comparisons using permutation techniques in FSL resulting in significance at pFWE< 0.05. During negative prediction error (mismatched taste) versus matched palatable taste, women showed increased BOLD response bilaterally in the central operculum (pFWE=0.002; k=1428; MNI: -55,-6,19 and pFWE=0.005, k=867; MNI: 60,-4,12). When viewing the sub-palatable versus the palatable cue, BMI was positively related to BOLD response in cingulate gyrus (pFWE=0.01, k=242; MNI: 12,-32,24). Results indicate the sub-palatable milkshake taste is salient, eliciting robust response in gustatory regions, and higher BMI was related to increased response to a sub-palatable cue in a region that encodes attentional processing. The positive relation between response to cues that signal a sub-palatable taste and BMI may reflect meaningful weight-related differences in sensitivity to cues predicting punishment.

10:30 - 11:00 AM	Calusa DE
Coffee Break	

11:00 - 12:00 PM	Calusa ABC
MARS LECTURE 2	

Chair(s): Dana Small

11:00 **Obesity, Roux-En-Y Gastric Bypass And Taste: A Peek Into The Brain.**

P.M. DI LORENZO[1], K. CZAJA[2], A. HAJNAL[3]

[1]Binghamton University, Binghamton, NY, United States, [2]University of Georgia Athens, Athens, GA, United States, [3]The Pennsylvania State University College of Medicine, Hershey, PA, United States

There is evidence that taste preferences and acuity change when an animal becomes obese. Reversal of obesity with Roux-en-Y gastric bypass (RYGB) surgery is accompanied by restoration of taste preference patterns to that of lean individuals. However, our understanding of the brain mechanisms that underlie these changes remains incomplete. Work in our lab and that of our collaborators has shown that a high fat diet induces changes in gut-brain communication and an inflammatory response in the brainstem. We studied the functional implications of these results by recording responses to taste stimuli in the nucleus tractus solitarius (NTS, the first central relay in the gustatory pathway) of awake, freely licking rats. Tastants included representatives of the 5 basic taste qualities: sucrose for sweet, NaCl for salty, citric acid for sour, caffeine for bitter and monosodium glutamate (MSG) for umami, as well as naturalistic counterparts to these taste qualities: grape juice for sweet, clam juice for salty, lemon juice for sour, coffee for bitter. We also tested cream as a fatty stimulus. Results showed that taste responses, especially to sweet stimuli, in the NTS of diet-induced obese (DIO) rats are blunted compared to those in lean animals. That is, there are proportionally fewer taste responses in DIO rats, they are smaller and shorter, and they occur at a longer latency than those in lean rats. DIO rats that undergo RYGB surgery and continue to be maintained on a high fat diet experience weight loss and normalized taste preferences, but deficiencies in NTS taste responsiveness do not recover. Collectively, these results suggest that a high fat diet can change the way in which the taste of food is encoded by the brain and that these changes are resilient to weight loss.

12:00 - 1:30 PM	Calusa Foyer
Lunch on Own	

Salads, Sandwiches, Hamburgers and Hot Dogs will be available for purchase by CASH or hotel room charge in the Calusa Foyer. Price Range ($10-$15)

12:15 - 1:30 PM	Captiva
New Investi(Alli)gator Luncheon	

NIAB invites you to join fellow students, post-docs, and new investigators for a New Investi(alli)gator luncheon. Come meet some new faces, as well as catch up with old friends at this informal networking event. Attendees that arrive at the session will receive a voucher for their lunch purchase at the SSIB pop-up lunch stand in Calusa Foyer.

1:30 - 3:30 PM	Calusa ABC
Symposium 2: Feeding on Protein	

Chair(s): Jamie McCutcheon and Mitch Roitman

1:30 **Protein Status Affects The Rewarding Value Of Meals Due To Their Protein Content To Maintain An Adequate Protein Intake**

D TOME
UMR PNCA, INRA, AgroParisTech, Université Paris-Saclay, Paris, France

Protein status, related to amino acid sufficiency in the body to support metabolic needs, is tightly controlled to prevent and counteract protein deficiency. In the underlying mechanisms, conditioning and learning processes relating signals from food characteristics and metabolic signals of sufficiency are integrated by the brain with a modulation of food motivation and components of feeding behaviour including food intake, food choice and food preference or aversion. Subjects learn to detect and avoid protein and amino acid-deficient diets through conditioned taste aversion. Protein deficient conditions, in contrast to protein sufficiency, are associated to high fasted ghrelin, low leptin levels, high hypothalamic *Npy* and *Crh* expression and high sensitivity of central dopamine-dependent reward pathways to the protein content of foods. Accordingly, a protein-rich diet induces a lower rewarding value of foods (satiating effect of protein) whereas a low-protein diet induces an increased motivation for food, a specific appetite for protein with preference for protein-rich foods and low rewarding value of low-protein foods that lead to maintain an adequate protein intake. In addition, particularly with no offered alternative food choice, a protein-deficient diets could, in some condition but not always, induce an increase in food intake inducing higher consumption of protein but also of energy as carbohydrates and fat which increases risk of fat deposition and adiposity (described as protein leverage) but this could also increase energy expenditure which moderates fat mass gain expected for the larger energy intake. These results challenge for a part the protein leverage concept that a marginally low protein diet induces significant increases food intake and body adiposity.

2:00 **Body Composition Is Predicted By Subtle Yet Measurable Differences In &Lsquo;Protein Valuation&Rsquo;**

JM BRUNSTROM[1,2], CM BUCKLEY[2], S AUSTIN[2], BM CORFE[3], M GREEN[4], EA WILLIAMS[3], AM JOHNSTONE[5], EJ STEVENSON[6]
[1]National Institute for Health Research, Bristol Biomedical Research Centre, University Hospitals Bristol NHS Foundation Trust and University of Bristol, Bristol, United Kingdom, [2]School of Experimental Psychology, University of Bristol, Bristol, United Kingdom, [3]Department of Oncology & Metabolism, The Medical School, The University of Sheffield, Sheffield, United Kingdom, [4]Department of Geography and Planning, School of Environmental Sciences, University of Liverpool, Liverpool, United Kingdom, [5]Rowett Institute, School of Medicine, Medical Sciences and Nutrition, University of Aberdeen, Aberdeen, United Kingdom, [6]Human Nutrition Research Centre, Institute of Cellular Medicine, Medical School, Newcastle University, Newcastle, United Kingdom

Protein is more satiating than carbohydrate and fat. However, it remains unclear whether macronutrients are equally valued. To explore this proposition, participants (N= 92) assessed 25 foods in 300 binary-choice trials. Total calorie content predicted choice. However, calorie-for-calorie, protein and carbohydrate influenced choice to a greater extent than fat (F(2,246)= 17.26, p< .001), suggesting an underlying difference in macronutrient ‘valuation.’ Importantly, participants varied considerably, and these differences were preserved in a second test session, one week later (week 1 vs week 2; protein r= .83, p< .001; carbohydrate, r= .90, p< .001; fat r= .90, p< .001). Many adults experience a loss of muscle mass as they age, and acute protein supplementation is known to improve muscle function. Therefore, we reasoned that fat-free mass might be predicted by protein valuation. In a second study we incorporated assessments of expected satiety and perceived healthiness as simultaneous predictors of choice. In this older sample (N= 91, range 40-85 y), protein was a better predictor (more valued) of choice than fat or carbohydrate (F(2,270)= 8.95, p< .001), and this remained the case after controlling for the weighting placed on expected satiety and healthiness (F(2,270)= 6.66, p=.002). As hypothesized (pre-registered), variation in this protein valuation positively predicted fat-free mass (β = 0.004, p< .001), after controlling for age, gender, and habitual protein consumption. By contrast, carbohydrate valuation was a negative (β= -.0.0003, p< .001) predictor. Together, these findings suggest that humans place a different value on calories derived from protein, carbohydrate, and fat, and that the tendency to value protein might offer protection from sarcopenia.

2:30 **Fgf21 Is An Essential Endocrine Signal For The Sensing Of Dietary Protein Restriction**

CD MORRISON
Pennington Biomedical Research Center, Baton Rouge, LA, United States

Restriction of dietary protein intake increases food intake and energy expenditure, reduces growth, and alters amino acid, lipid, and glucose metabolism. While these responses suggest that animals ‘sense’ insufficient consumption of amino acids, the basic physiological mechanism mediating this adaptive response is largely undescribed. Our work strongly suggests that the liver-derived metabolic hormone FGF21 coordinates the homeostatic response to dietary protein restriction. Circulating FGF21 levels are markedly increased by the restriction of protein or amino acid intake, and blocking the production of FGF21 or its signaling within the brain prevents adaptive changes in metabolism and behavior during protein restriction. FGF21 occupies a unique endocrine niche, being specifically induced when energy intake is adequate but protein and carbohydrate are

imbalanced. Collectively, the evidence suggests that FGF21 acts physiologically to coordinate metabolic and behavioral responses to dietary protein restriction.

3:00 **Distinct Patterns Of Neural Activity And Behavior Induced By Restriction Of Dietary Protein.**

G CHIACCHIERINI[1], KZ PETERS[1], F NANEIX[1], EMS SNOEREN[2], KP MYERS[3], JE MCCUTCHEON[1]

[1]University of Leicester, Leicester, United Kingdom, [2]UiT The Arctic Univ. of Norway, Tromsø, Norway, [3]Bucknell University, Lewisburg, PA, United States

Intake of dietary protein is tightly regulated across the animal kingdom. However, whether this regulation involves development of a specific appetite for protein when protein-restricted is still a matter of debate. In addition, the neural structures that allow protein intake to be regulated with respect to need state are not well defined. We have addressed these questions using a combination of behavior and calcium imaging fiber photometry. In our studies, rats on a protein-restricted diet develop a robust preference for protein, relative to carbohydrate; this preference is not seen in control, non-restricted, rats. Analysis of lick microstructure suggests that the elevated protein preference is due to an increase in palatability of protein, relative to carbohydrate. In addition, this preference appears to result from post-ingestive signals as we have shown conditioning to intragastric protein in protein-restricted rats. To uncover the circuits that underlie this preference, we used fiber photometry to measure neural activity in ventral tegmental area (VTA) during expression of protein preference. In protein-restricted rats we observed greater VTA activity when rats were consuming protein, relative to carbohydrate. Interestingly, when the diet was switched such that protein-restricted rats were allowed to replenish their protein levels, we saw a sustained behavioural preference for protein that continued to be reflected in elevated VTA activity. In contrast, in non-restricted rats that switched to protein-restricted diet we saw a rapid shift in preference and emergence of elevated VTA activity. These studies highlight interactions between the physiological need state for a specific macronutrient and aspects of innate and conditioned consummatory behavior.

1:30 - 3:30 PM	Calusa FGH
ORAL SESSION 4: Obesity and the Brain	

Chair(s): Kyle Burger and Uku Vainik

1:30 **Altered Synaptic Function In The Orbitofrontal Cortex With Diet Induced Obesity**

BK LAU, BP AMBROSE, M KAUR, C MURPHY-ROYALL, GRJ GORDON, SL BORGLAND
University of Calgary, Calgary, AB, Canada

The orbitofrontal cortex (OFC) receives sensory information about food and integrates these signals with expected outcomes. Thus, the OFC registers the current value of foods and updates actions based on this information. OFC lesions in animals show a lack of food devaluation. Interestingly, obese humans and rats fed a cafeteria diet have impaired devaluation of food rewards, implicating a potential obesity-induced dysfunction the OFC. Rats were given restricted (1h /day), extended (23h/day) or no (chow only) access to a cafeteria diet. Whole cell patch clamp electrophysiology was used to assess alterations in local inhibitory synaptic transmission onto pyramidal neurons. Rats became obese after 40- 45 days of extended, but not restricted access to a cafeteria diet. OFC pyramidal neurons from rats with extended access to a cafeteria diet had decreased inhibitory input partially due to an increase in MGluR1/5-dependent endocannabinoid signaling at inhibitory synapses onto pyramidal neurons. Furthermore, rats with extended access to a cafeteria diet exhibited increased extrasynaptic glutamate that could be restored with N-acetylcystein. Finally, we show increased astrocyte territory and cytokine production that may be associated with the obesogenic diet. Taken together, these data suggest that cellular adaptations in the lateral OFC are associated with extended but not restricted access to a cafeteria diet. Thus, obesity can alter function of OFC pyramidal neurons, which may underlie changes to goal-directed food seeking in obesity.

1:45 **Unifying The Many Neurocognitive Traits Associated With Obesity: Uncontrolled Eating**

U VAINIK[1,2], I GARCIA-GARCIA[1], A DAGHER[1]
[1]Montreal Neurological Insititute, McGill University, Montreal, QC, Canada, [2]Institute of Psychology, University of Tartu, Tartu, Estonia

Many eating-related psychological constructs have been proposed to explain obesity and over-eating. However, these constructs, including disinhibition, hedonic hunger, emotional eating, binge eating, food addiction, and the like all have similar definitions, emphasizing loss of control over intake. As questionnaires measuring the constructs correlate strongly (r>0.5) with each other, we propose that these constructs should be reconsidered to be part of a single broad phenotype: Uncontrolled Eating (UE). Such approach enables reviewing and meta-analyzing evidence obtained with each individual questionnaire. Here, we describe robust associations between UE, body mass index (BMI), food intake, psychological traits, and brain systems. We show that UE is phenotypically and genetically intertwined with BMI and food intake. Based on longitudinal findings, UE and BMI are somewhat separable phenomena, whereas UE and food intake seem more interchangeable. We also review evidence on how three independent psychological constructs may underpin UE: heightened food reward sensitivity, lower self-control, and higher negative affect. UE mediates all three constructs' associations with BMI and food intake. Finally, we review and meta-analyze brain systems subserving UE: namely, (i) the dopamine mesolimbic circuit associated with reward sensitivity, (ii) frontal cognitive networks sustaining dietary self-control, and (iii) the hypothalamus-pituitary-adrenal axis and amygdala circuits supporting stress responses. We conclude that treating different eating-related constructs as a single concept, UE, enables drawing robust conclusions on associations between UE, food intake and BMI, psychological variables, and brain structure and function.

2:00 **The Relation Among Food Insecurity, Obesity, And Delay Discounting For Food**

EB RASMUSSEN, LR RODRIGUEZ, D KYNE-RUCKER, BE PERSCHON
Idaho State University, Pocatello, ID, United States

The purpose of the present study was to determine the relation among food insecurity, obesity, and delay discounting (DD) for food and money. Food insecurity (FI) refers to inconsistent access and budget for foods that meet basic nutritional needs. Women from food insecure households are more likely to be obese than women from food secure households. DD, a behavioral measure of impulsivity, refers to a decrease in the subjective value of a reward as delay to its receipt increases. Previous research has also shown an association between food insecurity and DD for monetary outcomes. Further, DD has been linked to obesity, which suggests that the devaluation in delayed rewards may be an underlying process in the acquisition and maintenance of obesity. Ninety-two women were recruited from a community sample. Participants completed DD tasks for food and money and food security measures, and other measures related to intellectual functioning, demographics, and biometrics. Two mediation analyses were conducted to determine the extent to which DD for food or DD for money mediated the relation between FI and BMI. Analyses revealed FI significantly predicted DD for food (b=.12, SE=.06, p=.04) and money (b=.74, SE=.182, p< .001). However, DD for food or money did not significantly mediate the relation between FI and obesity. With DD removed from the models, FI significantly predicted

BMI (b=4.37, SE=1.95, p=.03). These results indicate a significant relation between FI and higher impulsivity, and FI and BMI. However, impulsivity may not necessarily be the mechanism that links higher FI with increases in BMI.

2:15 **Mindsets Influence Brain Response And Behavior During Pre-Meal Planning In Overweight And Obese Adults**

R VEIT[1], LI HORSTMAN[1], MA HEGE[1], M HENI[1], PJ ROGERS[2], JM BRUNSTROM[2], A FRITSCHE[1], H PREISSL[1], S KULLMANN[1]

[1]Institute for Diabetes Research and Metabolic Diseases, University of Tübingen, Tübingen, Germany, [2]Nutrition and Behaviour Unit, University of Bristol, Bristol, United Kingdom

Attentional processes play an important role in the decisions we make. Currently, it is not known whether pre-meal planning can be influenced by attentional processes in overweight and obese individuals. We investigated the neural underpinnings of pre-meal planning in 17 overweight/obese compared to 17 lean adults by means of fMRI. To investigate the important role of attentional focus, participants adopted different mindsets while selecting their portion size for lunch. Compared with a free choice condition, mindsets induced behavioral changes in portion size selection associated with specific neuronal processes and these changes were group specific. Compared to lean participates, overweight and obese participants showed a decreased response in the hypothalamus and ventral striatum in response to the healthiness and fullness mindset, respectively. In the pleasure mindset, however, overweight/obese participants showed a more prominent response in parts of primary gustatory cortex, which significantly correlated with portion size selection. Indeed, overweight/obese participants chose larger portion sizes during the pleasure mindset than the lean group. Understanding these behavioral differences during pre-meal planning can inform the development of effective strategies for heathy weight management.

2:30 **Optimizing A Test Battery For Neurocognitive Function In Obesity**

IH HOVENS, JR DALENBERG, EB ZENGIN, DM SMALL
Department of Psychiatry, Yale School of Medicine, New Haven, CT, United States

Obesity has been associated with reduced cognitive performance in a number of domains. However, there have been inconsistencies in findings and few studies have included comprehensive testing. Here we used the data from the Human Connectome Project, which includes 25 neurocognitive tests, to guide the development of a neurocognitive battery optimized for maximum assessment of affected domains in the minimum amount of time. We used the s1200 data release, excluding subjects with a BMI< 18.5 and a positive drug or alcohol test (n=953). All analyses were adjusted for age, sex, education, income, depression, sleep quality, and alcohol abuse. Statistics were FDR corrected. First, we correlated the neurocognitive test outcomes with BMI. This isolated 8 tasks, all showing negative correlations with BMI {oral reading recognition (p=0.013), matrix reasoning (p=0.039), line orientation (p=0.004), word memory (p=0.005), delay discounting (p=0.005), 0-back tool condition (p=0.024), the relational task (p=0.013) and its match control task (p=0.011)}. Next, we performed principle component analysis on the 25 test outcomes to determine which tests capture similar variance. Seven components were identified and subjected to linear regression models to determine their association with BMI. Three components were not correlated or only weakly correlated with BMI and were not considered further. From each of the remaining components the test that was most strongly associated with BMI was selected for the final battery. This resulted in a 35-minute battery including the Penn line orientation task (5 min), the delay discounting task (~20 min), the relational task (6 min) and the word memory task (4 min) that we recommend as a core neurocognitive test battery for obesity.

2:45 **Effects Of A 12-Week High Fat Diet On Brain, Behavior, And Perception In Healthy Humans**

AG DIFELICEANTONIO[1], S EDWIN THANARAJAH[2,3], K ALBUS[4], O CORNELY[4], JC BRUENING[2], DM SMALL[1], M TITTGEMEYER[2]

[1]Yale University, New Haven, CT, United States, [2]Max Planck Institute for Metabolism Research, Cologne, Germany, [3]Department of Neurology, University Hospital of Cologne, Cologne, Germany, [4]Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), Cologne, Germany

There is clear causal evidence from animal studies that a high fat diet can alter dopamine signaling and impair dopamine-dependent functions. Emerging work in humans also supports a causal relationship; though few studies collect comprehensive measures of diet, metabolism, and adiposity, which may all contribute to brain alterations. Here, we provide a preliminary report of an ongoing study where perceptual, metabolic, neural, and behavioral measures are collected before and after healthy-weight participants are assigned to consume either a high protein yogurt (~50% kcal from protein) or an equicaloric high fat (~40% kcal from fat) yogurt twice daily for 12-weeks. Despite no change in adiposity or metabolic measures, diet influenced fat preference and brain response to a high fat/high sugar milkshake. More specifically, preference for low fat, but not low sugar foods decreased in the high fat, but not high protein group and striatal response to milkshake decreased in the high fat, but not the high protein group. Increased responses were also observed in the high fat group in the midbrain in response to the milkshake cue and in the amygdala in response to the milkshake (trend, preliminary analysis). Diet had no influence on a measure of impulsive responding. This preliminary analysis supports a causal influence of a high fat diet on fat preference and on neural circuits responding to palatable food cues.

3:00 **Endocannabinoid Metabolism In The Mouse Upper Small Intestinal Epithelium Is Dysregulated In Diet-Induced Obesity**

DA ARGUETA, NV DIPATRIZIO
Division of Biomedical Sciences, School of Medicine, University of California Riverside, Riverside, CA, United States

Endocannabinoids (eCBs) are lipid-derived signaling molecules produced in the brain and peripheral organs, and control feeding behavior and energy homeostasis. We reported that eCB signaling at cannabinoid 1 receptors (CB_1Rs) in the upper small intestinal epithelium is upregulated in western diet-induced obese mice (DIO; chronic exposure to a high fat-sucrose diet) and is critical for overeating associated with DIO (i.e., increased caloric intake, meal size, and rate of feeding). For example, inhibiting peripheral CB_1Rs with AM6545, a peripherally-restricted neutral CB_1R antagonist, completely normalized meal patterns in DIO mice to control levels, which suggests overactive eCB signaling in the gut drives hyperphagia. In order to identify key components of the eCB system that are dysregulated in DIO and lead to overactive eCB signaling, we developed a highly sensitive ultra-performance liquid chromatography/tandem mass spectrometry-based method (UPLC/MS^2) to analyze activity of biosynthetic (i.e., diacylglycerol lipase, DGL) and degradative enzymes (i.e., monoacylglycerol lipase, MGL) involved in metabolism of the abundant eCB, 2-AG. When compared to male mice fed a low fat-sucrose diet, DIO mice fed western diet for 60 days had elevated levels of 2-AG in upper small intestinal epithelium (45.7 ± 6.9 to 92.6 ± 16.4 nmol per g tissue), which was met with increased activity of DGL (0.12 ± 0.02 to 0.22 ± 0.03 nmol product per mg tissue per minute) and MGL (36.3±3.8 to 51.6±4.9 nmol product per mg tissue per minute). Our results suggest that the eCB system in small intestinal epithelium is remodeled after chronic exposure to diets high in fats and sugars, which may in turn, modify a setpoint of gut-brain signaling important for food intake and promote overeating.

3:15 **Sexually Dimorphic Action Of Nts Astrocytes In Leptin-Mediated Energy Balance And The Development Of Obesity**

LM STEIN, R LHAMO, AN CORINI, AE REED, MR HAYES
University of Pennsylvania, Philadelphia, PA, United States

Astrocytes within the nucleus tractus solitarius (NTS) are hypothesized to modulate the energy balance effects of leptin; dysregulation of which may potentially contribute to the development of obesity and leptin resistance. Here, we examine *in vivo* and *in vitro* the contribution of diet and sex on NTS astrocyte-leptin signaling. Adult male and random-cycling female rats were maintained on either a chow or high-fat diet (HFD) (n=10-12/sex).

At dark onset, animals were treated with the glia-specific inhibitor fluorocitrate (FC; 5nmol; 4^{th} icv) or vehicle, followed by 4th icv 5µg/µL leptin or vehicle. In chow-fed males, but not females, FC attenuated both the hypophagia and body weight reduction produced by hindbrain leptin administration. Male and female rats on HFD exhibited a diminished anorectic response to leptin administration alone, for which FC pretreatment had no effect. To determine whether HFD-induces hindbrain astrogliosis, rats (n=6/diet/sex) were placed on chow or HFD for 4 weeks and gliosis was measured by glial-fibrillary acidic protein (GFAP) IHC. Chronic HFD exposure resulted in a significant increase in NTS GFAP in males, but not females, further highlighting the sexually dimorphic NTS astrocytic response to a HFD. Finally, we isolated NTS primary astrocytes from male or female pups (PD11) that were reared from dams maintained on HFD or chow. *In vitro* chronic (24h) exposure to 100ng/mL leptin significantly upregulated astrocyte-specific glutamate transporters (GLT1 and GLAST) and LepRb mRNA only in chow-male primary astrocytes. Collectively, these findings substantiate a sexually dimorphic role of NTS leptin signaling on astrocytes in energy balance regulation and the maladaptive changes that occur following HFD exposure.

3:30 - 4:00 PM	Calusa DE
Coffee Break	

4:00 - 6:00 PM	Calusa ABC
Symposium 3: New Insights Into Anorexia	

Chair(s): Tim Moran & Nu-Chu Liang

4:00 **Examining Weight Suppression As A Transdiagnostic Factor Influencing Illness Trajectory In Eating Disorders**

PK KEEL[1], LP BODELL[2], KJ FORNEY[1], J APPELBAUM[1], DL WILLIAMS[1]

[1]Florida State University, Tallahassee, FL, United States, [2]University of Chicago, Chicago, IL, United States

The first diagnostic criterion for anorexia nervosa (AN) is medically low weight. For most patients, this reflects a weight that is well below their highest lifetime weight – a state referred to as weight suppression (WS). Although low weight is a central defining feature for AN, recent research indicates that WS has relevance for understanding illness trajectory across eating disorders, including AN, bulimia nervosa, and binge-eating disorder. Through a series of studies, we have developed a model to explain the link between WS and illness trajectory in eating disorders. Our model posits that WS contributes to reduced circulating leptin, which leads to reduced postprandial glucagon-like peptide 1 (GLP-1) response. Diminished leptin and GLP-1 function contribute to alterations in two reward-related constructs in the Research Domain Criteria (RDoC): approach motivation and sustained responsiveness to reward. Respectively, these changes increase drive/motivation to consume food (approach motivation) and decrease ability for food consumption to lead to a state of satiation/satisfaction (sustained responsiveness to reward). Combined, these alterations increase risk for experiencing large, out-of-control binge-eating episodes. In addition, we have shown that WS predicts increased drive for thinness, above and beyond its influence on bulimic symptoms, which further contributes to illness trajectory across eating disorders. This talk presents new data examining the biological and psychological sequelae of WS within this model. Identification of transdiagnostic biobehavioral predictors of illness trajectory can contribute to novel interventions that improve course and outcome across disorders.

4:30 **Brain Reward Circuit Alterations Are Central To The Pathophysiology Of Anorexia Nervosa**

G.K. FRANK[1,2], M.C. DEGUZMAN[1,2]

[1]Department of Psychiatry, School of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO, United States, [2]Neuroscience Program, University of Colorado Anschutz Medical Campus, Aurora, CO, United States

Anorexia nervosa (AN) is associated with adolescent onset, severe low bodyweight and high mortality rate. Self-starvation and fear of weight gain, despite severe underweight and risk of death, have been puzzling. Here we wanted to test whether there is evidence that altered brain reward response in AN has a central function in predicting treatment response, explaining top down striatal-hypothalamic brain connectivity, and driving elevated harm avoidance in AN. We recruited fifty-six adolescents with AN (mean age=16.6±2.5 years, mean BMI=15.9±0.9 kg/m^2) and fifty-two control adolescents (mean age=16.0±2.8 years, mean BMI=20.9±2.1 kg/m^2). During brain imaging, participants completed a sucrose taste reward paradigm, where violations of learned associations between visual and taste stimuli evoked the dopamine-related prediction error (PE). Effective connectivity during sweet taste receipt investigated hierarchical brain activation across the brain-network that regulates eating. PE response was elevated in adolescents with AN in caudate, insula and orbitofrontal cortex. Orbitofrontal PE response correlated positively with harm avoidance, but negatively with weight gain and discharge body mass index. While controls showed a bottom-up connectivity from hypothalamus to ventral striatum, the opposite was noted in AN and insula and orbitofrontal PE response was positively correlated with effective connectivity strength in AN from ventral striatum to hypothalamus. These results provide a link between altered PE response and previously found elevated harm avoidance and drive for thinness, as well as top-down brain connectivity in AN. We propose that food restriction driven elevated PE in AN has a central role in driving anxiety and top down controlled food avoidance.

5:00 **Anorexia Nervosa: Behavioral And Neurobiological Insights From Animal Models**

KL TAMASHIRO
Johns Hopkins University School of Medicine, Baltimore, MD, United States

Anorexia Nervosa (AN) is a serious behavioral psychiatric disorder with high morbidity and mortality characterized by self-starvation. Animal

models cannot mimic the full phenomenology and symptomatology of the condition, but provide tools with which to potentially determine the underlying neurobiology. Activity-Based Anorexia ("ABA") is an animal model that mimics key features of AN and can be used to investigate the potential neural consequences of symptoms of AN since key aspects of the disorder are present: severe food restriction, excessive exercise, and weight loss. Although the etiology of AN is multifactorial, evidence supports a strong genetic and environmental contribution to individual vulnerability to this disorder. We found that a subset of female rat offspring that experienced prenatal stress (PNS) lose more weight in the ABA paradigm which is attributable to greater hypophagia and failure to upregulate AgRP and orexin in the hypothalamus compared to weight matched controls. Epigenetic programming during development may contribute to the greater susceptibility in PNS offspring. Physiological consequences of starvation, including dysregulation of neuropeptides controlling appetitive drive and in neural reward circuits, both of which are implicated in AN, may sustain motivated food restriction and hyperactivity characteristic of the disorder. Female rats that experienced ABA, but were weight-recovered when tested, acquired a conditioned taste aversion faster, were slower to extinguish the aversion behavior, and display persistent cognitive deficits and anxiety-like behavior. Animal models such as ABA are useful for elucidating those factors that may predispose or perpetuate behaviors that contribute to AN etiology.

5:30

Identifying Novel Therapeutic Targets For Anorexia Nervosa

LM ZELTSER
Columbia University, New York, NY, United States

There is an urgent need to develop new strategies to treat anorexia nervosa (AN), because there are no medications that impact the life-threatening restrictive feeding behaviors that cause severe weight loss. A major obstacle to achieving this goal is the lack of animal models that recapitulate the pattern of disease onset typically observed in human populations. We developed a novel translational mouse model to study interactions between genetic, psychosocial and biological risk factors that promote anorexic behavior. This model incorporates several factors that are consistently associated with increased risk of anorexia – adolescent females, genetic predisposition to anxiety imposed by the *Brain-derived growth factor* (*BDNF)*-Val66Met gene variant, social stress and caloric restriction. We are beginning to identify signaling pathways in the brain that drive anorexic behavior in our model, with the ultimate goal of identifying novel therapeutic targets for anorexia.

4:00 - 6:00 PM	Calusa FGH
ORAL SESSION 5: Reward and Cue Responsivity	

Chair(s): Liz Mietlicki-Basse and Stephanie Kullman

4:00 **Activation Of Amylin Receptors In The Ventral Tegmental Area Reduces Cocaine Taking And Seeking In Rats.**

Y ZHANG[1,2], CA TURNER[1,2], HD SCHMIDT[1,2]

[1]Department of Biobehavioral Health Sciences, School of Nursing, University of Pennsylvania, Philadelphia, PA, United States, [2]Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States

Amylin is a peptide hormone co-secreted with insulin from pancreatic β-cells. Amylin crosses the blood brain barrier and activates amylin receptors expressed throughout the brain. Amylin receptors are heterodimeric protein complexes consisting of a calcitonin receptor (CTR-A or B) and one isoform of a receptor activity-modifying protein (RAMP1-3). Central amylin signaling has been shown to regulate food intake. Specifically, activation of amylin receptors in the mesolimbic dopamine system has been shown to reduce the hedonic value of food. Given that the reinforcing effects of natural rewards and drugs of abuse are regulated by the mesolimbic dopamine system, these findings suggest that central amylin signaling may play an important role in addiction-like behaviors. The goal of these studies was to determine the role of amylin receptors expressed in the ventral tegmental area (VTA) in the voluntary cocaine taking and cocaine-seeking behavior. Administration of amylin (0.4 μg) directly into the VTA attenuated cocaine self-administration and cocaine priming induced reinstatement in rats, without altering standard chow intake, body weight, and locomotor activity. In addition, we investigated the effects of voluntary cocaine taking and subsequent withdrawal on expression of amylin receptors in the VTA. Our results indicate that, following one day of withdrawal from voluntary cocaine taking, RAMP3 expression was decreased in VTA. In contrast, CTR-A expression was elevated in VTA following seven days of withdrawal. These findings identify a dynamic process wherein cocaine regulates amylin receptor expression in the brain. Taken together, these findings demonstrate an important role for central amylin receptors in preclinical models of cocaine addiction.

4:15 **Circuit-Specific Knockdown Of ΔFosb Gene In Ventral Hippocampal Projections Augment Food-Seeking And Cue-Potentiated Feeding**

AL EAGLE[1], NM RUSSELL[2], R GIFFORD[2], AJ ROBISON[1], AW JOHNSON[2]

[1]Department of Physiology, Michigan State University, East Lansing, MI, United States, [2]Department of Psychology, East Lansing, MI, United States

The transcription factor ΔFosB is a truncated product of the *FosB* gene induced by chronic neuronal activity and notable for its stability, making it a key mediator of long-lasting gene expression changes in the brain. ΔFosB is elevated in response to prolonged intake of palatable food, and its overexpression in the nucleus accumbens (NAc) is sufficient to increase sucrose intake. In the current study, we utilized a novel dual-virus CRISPR-Cas9 system to knockdown the *FosB* gene in specific ventral hippocampal (vHPC) projections, as vHPC has recently been implicated in the control of higher-order features of feeding behaviors. In two separate studies, we targeted two distinct vHPC ΔFosB projections—those to the amygdala (AMY) and NAc. We injected a retrograde HSV expressing Cas9 into the AMY or NAc of B6 mice, followed by injections into the vHPC of a traditional HSV expressing a gRNA that targets the first exon of the *FosB* gene. Thus, only neurons that project from vHPC to the AMY or NAc expressed both the gRNA and Cas9, resulting in knockdown of ΔFosB expression in vHPC cells specifically projecting to these target regions. To examine the behavioral implications of ΔFosB knockdown in these separate circuits, vHPC-AMY and vHPC-NAc B6 mice underwent a range of behavioral tests to assess food-seeking, consumption and metabolic phenotyping. Overall, vHPC-AMY ΔFosB knockdown enhanced learned overeating behaviors as assessed by cue-potentiated feeding, whereas vHPC-NAc knockdown resulted in a significant increase in lever responding for food and altered body composition. These findings suggest that projection-specific *FosB* gene silencing in vHPC projections underlies dissociable components of appetite control.

4:30 **The Effect Of Satiation On Cognitive Processes**

MS SPETTER[1], P ROTSHTEIN[1], JM THOMAS[2], CT DOURISH[3], M HALLSCHMID[4], M LEE[5], S HIGGS[1]

[1]School of Psychology, University of Birmingham, Birmingham, United Kingdom, [2]Department of Psychology, Aston University, Birmingham, United Kingdom, [3]P1vital, Manor House, Howbery Park, Wallingford, Oxfordshire, Wallingford, United Kingdom, [4]Institute for Medical Psychology and Behavioural Neurobiology & German Center for Diabetes Research (DZD), University Tübingen, Tübingen, Germany, [5]Department of Psychology, College of Human and Health Sciences, Swansea University, Swansea, United Kingdom

Natural satiation attenuates activity in reward-related brain regions and increases activity in cognitive control areas, but little is known about the specific underlying cognitive processes. This study assessed the effect of satiation on reward, memory and behavioural control processes. Twenty-

seven participants (10 male, BMI 22 kg/m^2, age 21y) were tested on 2 separate test days, either after eating a meal to satiation or after not eating for 4 h (satiated vs. premeal: order counterbalanced). They completed a battery of cognitive tasks, measuring both behavioural and BOLD-fMRI responses. Food images (but not non-food images) were rated as less appealing in the satiated condition ($p< 0.001$). Choice of a delayed food reward in a delay discounting task was increased in the satiated condition ($p=0.005$), whereas there was no effect of satiation on monetary reward choice ($p=0.9$). In a Go-NoGo task assessing impulsive responding and attention, there were more omission errors (a failure to respond on a go-trial) in the satiated condition ($p=0.01$) suggesting reduced attention to the go stimuli. Free recall for food and non-food words was unaffected by nutritional state ($p=0.5$). These results suggest that satiation shifts preference from immediate to future food rewards and reduces attention to salient stimuli. The next step is to investigate the mediating neural mechanisms.

4:45 **Interoceptive Awareness Tasks Differentially Predict Resting-State Network Activity**

TN ATTUQUAYEFIO, JF BRUNSTROM, JCW BROOKS, JL FIELDING
University of Bristol, Bristol, United Kingdom

Food-choice may depend on the correct interpretation of bodily signals, *e.g.*, sensations of fullness. Interoception - the ability to consciously perceive inner bodily signals (*e.g.*, heartbeat), may provide the neural substrate for such decisions. We hypothesised that greater connectivity between the insula and resting-state networks might convey an improved ability to perceive internal states. In a within-subjects design, 38 females ($M = 22.4$ y) completed (i) a heart-rate detection task, (ii) water-load task and (iii) a food-choice task with stimuli varying in expected satiety and palatability. Resting-state functional magnetic-resonance imaging (rs-fMRI) data were acquired with a multi-band echo planar acquisition (TE/TR = 39/735 ms) on a 3T Siemens Skyra for a total of 490 volumes. Following pre-processing, group independent components analysis (ICA) identified 18 components. Dual regression analyses were used to determine inter-subject correlations between estimated components and measures of interoception and food choice. Participants with greater sensitivity in the water-load task ($M = 420.0$ ml; $SD = 223.4$) contributed more to the somatosensory network and had better connectivity between this network and the left anterior insula. Additionally, participants who performed well in the heart-rate detection task ($M = 0.73$; $SD = 0.26$) showed better connectivity between the posterior cingulate cortex and the default mode network. Meanwhile, functional connectivity was not associated with the relative importance of expected satiety and palatability in determining individual food choices. The findings here show that, while food choices were not linked to functional connectivity, better interoceptive awareness is associated with functional connectivity to the insula.

5:00 **Hypothalamic Interleukin-6 Is Necessary For Food-Motivated Behavior And Body Weight Regulation.**

L LóPEZ-FERRERAS[1], KK EEROLA[1], OT SHEVCHOUK[1], D MISHRA[1], M TUZINOVIC[1], KP SKIBICKA[1,3]

[1]1Institute for Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden, [2]2Wallenberg Centre for molecular and translational medicine, University of Gothenburg, Gothenburg, Sweden

Recent studies suggest that brain-produced interleukin-6 (IL6) is a necessary component of gut/fat to brain communication. IL6 is engaged by a wide variety of peripheral or central signals regulating energy homeostasis. For example, we previously showed that it is critical for the hypophagia and weight loss effects of GLP-1 agonist, exendin-4. Neuroanatomical substrates and mechanisms of IL6 energy balance control remain poorly understood. Here we investigated the role of IL6 on food intake and food reward in the lateral hypothalamus (LH). Microinjections of IL6 into the LH reduced chow and palatable food intake in male rats. In contrast, female rats responded with reduced motivated behaviour for sucrose, measured by the progressive ratio operant conditioning test. To test whether IL6 produced in the LH is necessary for normal ingestive and motivated behaviour, and body weight homeostasis we infused AAV-siRNA-IL6 into the LH to knock down the IL6 gene expression. This resulted in a potent (over 50%) increase in sucrose-motivated behaviour, without any effect on ingestive behaviour or body weight in female rats. In contrast, the treatment did not affect any parameters measured (chow intake, sucrose-motivated behaviour, locomotion, and body weight) in males. However, when males were challenged with a high-fat/high-sugar diet the LH IL6 knockdown rats rapidly gained more weight than control rats, starting at 7 days after diet exposure. This was likely driven by increase food intake. Together our data suggest that LH-produced IL6 is necessary and sufficient for ingestive behaviour and weight homeostasis in males. While in females, IL6 in the LH plays an important role in food motivated, but not ingestive behaviour or weight regulation.

5:15 **Hedonic Signatures Encoded In The Amygdala Implicitly Modulate The Motivational Value Of Food**

LJ TIEDEMANN, J BECK, A ALINK, K GIESEN, C BUECHEL, S BRASSEN
University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Neural mechanisms involved with the hedonic properties of food (referred to as ‘liking’) and those involved with motivating the desire for the food (referred to as ‘wanting’) are considered two separate mechanisms that act in concert to modulate eating behaviors (Berridge, 2009). In order to extract the neural signature of implicit hedonic processes and isolate its impact on motivational food value computation in humans we analyzed fMRI data acquired during a food-liking and a food-wanting task on two separate days including the identical stimulus sets in 30 young participants with

normal waist circumference according to WHO criteria. Significant variability in the willingness to consume foods ('wanting') could be explained by the likability of items (r = .61, P < .001). Using univariate as well as representational similarity analyses we could show: i) individual, trial-specific amygdala activation patterns encode the hedonic signature of foods during explicit food liking; ii) the reinstatement of this item-specific 'liking' pattern predicts the impact of hedonic properties on real decisions about food consumption; and iii) computation of wanting values in the ventromedial prefrontal cortex incorporates hedonic signals from the amygdala and hedonic-independent signals from the nucleus accumbens. Our findings highlight the distinct involvement of predominantly opioidergic systems in the implicit valuation of hedonic food properties and its impact on the motivational salience of food.

5:30 **(Nita Award Winner) Orexin/Hypocretin System Preferentially Drives Food Motivation In Female Rats Experienced With Excessive Weight Gain And Binge-Like Eating.**

MH JAMES[1,2], S LIU[1], S WALSH[1], BL YEOMANS[1], HE BOWREY[1,3], G ASTON-JONES[1], NT BELLO[1]

[1]Rutgers, The State University of NJ, New Brunswick, NJ, United States, [2]The Florey Institute of Neuroscience and Mental Health, Parkville, Australia, [3]Save Sight Institute, University of Sydney, Sydney, Australia

Binge eating behavior is characterized by recurrent episodes of rapidly consuming large quantities of calorie-dense food. Binge eating without compensatory behaviors is often associated with obesity. The hypothalamic orexin/hypocretin system is a critical regulator of pathological reward seeking, particularly for drugs of abuse. However, its role in compulsive food seeking is not well understood. Our hypothesis was that a consequence of binge-like eating would be disruption of orexin signaling relevant to food motivation. In addition, we examined the role of obesity on our outcomes. Sucrose demand was assessed using a novel behavioral economics paradigm to discern motivational and hedonic properties. Using a within subjects design, female Long-Evans rats (n=16) were assessed for baseline sucrose demand. Binge-like eating was induced by exposing rats to sweetened fat (vegetable shortening/10% sucrose) for 30 min, twice/week for 4w, before being re-assessed for sucrose demand and following injections of the orexin-1 receptor antagonist SB-334867 (0,10,30mg/kg;ip). Rats were then exposed to a high fat diet (HFD; 45% fat) for 8w, and the experiment was repeated. Sweetened fat binge intake was measured following SB dosing. Binge eating increased sucrose demand only after HFD-exposure, which was dose-dependently reversed by SB. Binge intake was not altered by HFD exposure. SB also decreased sweetened fat binge intake after HFD exposure. Our findings indicate an interaction between binge-like eating and excessive weight gain with respect to motivation for food. This effect was blocked by an orexin receptor-1 antagonist. Thus, the orexin system may be a potential target for novel pharmacotherapies for controlling overeating episodes in individuals with obesity.

5:45 **Healthier Food Reward-Hedonic Responses After Gastric Bypass Surgery Correlate With Weight Loss But Not Decreases In Insulin Resistance**

L FLORES, N CHHINA, T PARASTIKA, B ZAKI, N ONOKWAI, AP GOLDSTONE
PsychoNeuroEndocrinology Research Group, Neuropsychopharmacology Unit, Centre for Psychiatry, Division of Brain Sciences, Imperial College London, Hammersmith Hospital, London, United Kingdom

Roux-en-Y gastric bypass (RYGB) surgery switches preference from high-energy (HE) to low-energy (LE) foods, and reduces brain reward system activation during evaluation of HE vs. LE foods, aiding weight loss. A potential mechanism behind these changes is increased central actions of insulin, via reductions in insulin resistance. Obese patients (n=14, 13 female, age median 49y [range 31-63], BMI 45.9 kg/m^2 [38.9-50.9], n=5 T2DM) had fasted fMRI scans before and ~15 weeks post RYGB to measure BOLD signal in ROIs (orbitofrontal cortex (OFC), amygdala, caudate, putamen, nucleus accumbens, anterior insula) during evaluation of HE and LE food pictures to assess anticipatory food reward, and measurement of insulin resistance using fasting HOMA-IR. RYGB reduced weight by 21.9 kg [20.4-31.1], while HOMA-IR decreased from 3.10 [1.35-7.86] to 1.01 [0.77-3.06] (P=0.001) at 14.9 weeks [11.0-17.4] post-RYGB. Weight loss was positively correlated with the increase in appeal of LE foods (vs. objects) (r=+0.72, P=0.003), and increase in BOLD signal in amygdala and OFC to LE foods (r=+0.56, P=0.049; r=+0.67, P=0.012, n=13). Weight loss was not significantly correlated with decrease in HE foods (P=0.98), or decrease in BOLD signal in amygdala or OFC to HE foods (P=0.86-0.96). Decreases in HOMA-IR were not significantly correlated with changes in appeal rating, or BOLD signal in any ROI, to either HE or LE foods. Healthier food reward-hedonic responses after RYGB are related to weight loss, but not to reductions in insulin resistance, and interestingly this is driven by enhanced responses to LE, rather than reduced responses to HE foods. Ongoing studies are examining the role of changes in appetitive gut hormones, including PYY, GLP-1 and ghrelin.

6:00 - 8:00 PM	Calusa DE
POSTER SESSION II	

P39 **Olfactory Bulbotomy In Wild Type And T1R2+T1R3 Knockout Mice Severely Blunts Concentration-Dependent Responsiveness To Maltodextrin And Sucrose In A Brief Access Test.**

C INUI-YAMAMOTO[1], GD BLONDE[1], LA SCHIER[2], AC SPECTOR[1]

[1]Department of Psychology and Program in Neuroscience, Florida State University, Tallahassee, FL, United States, [2]Department of Biological Sciences, University of Southern California, Los Angeles, CA, United States

Mice lacking the taste receptor for sweeteners (T1R2+T1R3 heterodimer) display concentration-dependent behavioral responsiveness to maltodextrin solutions, such as Maltrin, in taste tests. Here we examined the necessity of central projections from the olfactory bulb in the maintenance of responsiveness to Maltrin (1-32%) and sucrose (1-32%) in T1R2+T1R3 knockout (KO) and C57BL/6J wild type (WT) mice in a series of 30-min brief access (10-s trials) licking tests. Concentration-dependent licking of Maltrin and sucrose were severely blunted in both KO (n=12) and WT (n=11) mice with functionally (buried potato chip test) and histologically confirmed bulbotomies (BULB) relative to their sham-operated counterparts (SHAM-KO, n=12; SHAM-WT, n=12). The fact that bulbotomy markedly decreased licking for sucrose in WT mice during trials in which access to the stimulus is limited to a few seconds suggests that surgical disconnection of the olfactory bulb from the forebrain is sufficient to substantially attenuate orally induced ingestive motivation for the carbohydrate stimuli tested here, including those that normally activate the T1R2+T1R3 receptor. Whether bulbotomy affects the sensory-discriminative features of these stimuli such as their detectability and perceived quality, remains to be tested. These results underscore the importance of understanding taste function in a broader context that involves the contribution of diverse sources of chemosensory input.

P40 **Effects Of A Common Single Nucleotide Polymorphism Of The Mu-Opioid Receptor (*Oprm1* A112G) On Fat Preference And Taste Responses In Mice.**

BLY SACHDEO[2], GM GIUNTA[1], A BADRINATH[1], A TYRYLLO[1], NT BELLO[1,2]

[1]Department of Animal Sciences, Rutgers, The State University of New Jersey, New Brunswick, NJ, United States, [2]Nutritional Sciences Graduate Program, Rutgers, New Brunswick, NJ, United States

A common single nucleotide polymorphism (SNP) of the mu-opioid receptor gene (*Oprm1* A118G) results in a functional amino acid substitution (N40D) at a putative N-glycosylation site. Although this SNP has been associated with alterations in reward guided behaviors, it is unknown whether this SNP influences taste and experience-based taste outcomes. Transgenic mice expressing the homologous SNP (A112G) were used to explore taste sensitivity in homozygous female mice (n =7 or 8/genotype) using an automated gustometer ("Davis Rig") to measure taste response to varying concentrations of glucose, fructose, Intralipid®, alanine, sodium chloride, citric acid, monosodium glutamate, and quinine hydrochloride. GG mice had lower mean lick numbers at the highest sucrose concentration (1.5M) and fructose concentrations (0.3M, 1M; $p < 0.05$). In another set of experiments, male A112G mice were exposed to a dietary-induced binge eating protocol. Six-week-old homozygous male mice randomized to four feeding schedules, including Restrict-Binge, Binge, Restrict, and Naive (n=8/group/genotype), were provided with intermittent access (30 min) to a highly palatable "binge" food (vegetable shortening/10% sucrose) twice weekly, with or without food restriction (24 h) for 6 wks. Following this, mice underwent a 2-bottle 48 h preference test for 5% Intralipid® and water. Naive GG mice had a lower preference score (Lipid Intake/Total Intake; $p < 0.05$) for 5% Intralipid®. Our findings indicate the mouse homolog of the A118G SNP is associated with altered taste responses for high sugar concentrations in female mice. Although naive male mice had a lower preference for 5% Intralipid®, previous binge-like feeding did not differentially alter fat preference between genotypes.

P41 **Salivary Proteins Can Suppress Negative Oromotor Responses To Quinine**

LE MARTIN, KE KAY, A-M TORREGROSSA
SUNY University at Buffalo, Buffalo, NY, United States

Our lab has previously shown that animals exposed to quinine upregulate a sub-set of salivary proteins (SPs), and those with the SPs upregulated have increased rates of feeding on a quinine diet and increased brief-access licking to intermediate concentrations of quinine. These studies suggest that the SPs alter orosensory feedback; however, they rely on SPs upregulated by diet exposure and cannot control for the role of experience. Here we use taste reactivity to determine if SPs are able to alter bitter taste in animals with no previous bitter diet experience. First, saliva with proteins stimulated by injections of isoproterenol was collected from anesthetized rats. This "donor saliva" was analyzed for protein concentration and profile and used either unfiltered (protein-containing saliva, PCS) or filtered of proteins (protein-filtered saliva, PFS). Bitter-naïve rats were implanted with oral catheters and infused with one of several solutions (1mM quinine dissolved in water, PCS, PFS, and artificial saliva or each solution alone). Their orofacial

movements were videotaped, and videos were scored. There is no significant difference in responses when animals are infused with PCS or PFS alone, but animals made fewer negative responses when infused with quinine in PCS than when they were infused with quinine in PFS ($p = 0.003$). This suggests that the presence of SPs is sufficient to reduce negative responding to quinine.

P42 **Bitter Tastants Stimulate Gastric Acid Secretion From The Human Gastric Cancer Cells**

HY KIM
Korea Food Research Institute, Wanju-gun, South Korea

Prior to the modern era of medicine, fluid preparation derived from bitter tasting plants were given to promote appetite and thus to aid digestion. Today, the treatment of digestive disorders with bitter tastants continues in Asia and Europe. However, the exact mechanisms that could be involved in digestive processes by bitter tastants have yet been scientifically investigated. Meanwhile, for most of the bitter ligands, the interactions with 25 human bitter taste recepors (the taste receptor 2 family; TAS2Rs) have been reported. In this study, it was investigated the possible effects of 23 bitter tastants on stimulation of gastric acid secretion, crucial of digestive processes, using human gastric cancer cells (HGT-1) by means of a pH-sensitive fluorescent dye which determines the intracellular pH as an indicator of proton secretion. Among the tested tastants, naringin (a flavanone derived from citrus fruits), aloperine (a quinolizidine alkaloid derived from traditional Chinese herb Sophora flavescens Ait) and cromolyn (an anti-inflammatory drug used for prophylactic treatment of bronchial asthma and allergic rhinitis) revealed their inducing effects in gastric acid secretion. Naringin and aloperine have not been characterized by which the bitter taste receptors belonging to the taste receptor 2 family (TAS2R) are activated. Cromolyn has been known to activate TAS2R7, -R43 and –R49. In conclusion, naringin, aloperine and cromolyn might be involved in digestive processes or appetite-stimularory effect.

P43 **Effects Of Chronic Glucagon-Like Peptide-1 Receptor Agonism On Sucrose Licking Microstructure In Male Rats.**

T INUI[1], K HYDE[1], G BLONDE[1], C MATHES[2], A SPECTOR[1]

[1]Department of Psychology and Program in Neuroscience, Florida State University, Tallahassee, FL, United States, [2]Department of Psychology and Program in Neuroscience, Baldwin Wallace University, Berea, OH, United States

Stimulation of the glucagon-like peptide-1 (GLP-1) receptor decreases body weight, is thought to promote satiation, and may contribute to the beneficial effects of Roux-en-Y gastric bypass (RYGB). In rats, acute systemic administration of the GLP-1-receptor agonist exendin-4 (Ex-4) decreases sucrose intake, as does RYGB. To clarify the effects of long-lasting stimulation of GLP-1 receptors on sucrose drinking, we subcutaneously implanted intact male rats with osmotic minipumps containing Ex-4 in saline, which delivered the drug at a rate of 0, 1, 3, or 10 µg/kg/day (n=8/group). Five days after pump implantation, the rats were exposed, in a counterbalanced crossover design, to sucrose (0.1, 0.3, or 1.0 M) in a gustometer for 60 min under either 22-h food-deprived or ad lib conditions. We assessed the microstructural lick patterns during the first meal (licks before a 5-min pause). Only the highest dose significantly decreased body weight and total caloric intake (food + sucrose over 24h). Even at the highest dose, we found little effect of Ex-4 on the number or size of the bursts (separated by pauses >1 s) during a single sucrose meal regardless of the concentration. In general, drug treatment did not compromise the ability of rats to respond to fasting or sucrose concentration in a prototypical manner. Our results suggest that chronic administration of Ex-4, at least under these test conditions, does not impact motivational processes driving sucrose ingestion across a broad concentration range regardless of food deprivation state.

P44 **Nicotine Elicits Ingestive And Aversive Taste Reactivity Responses In Male And Female Rats**

LE RUPPRECHT, NA ADDY
Yale University School of Medicine, New Haven, CT, United States

The abuse liability of tobacco products depends on the rapid absorption of nicotine into the blood and brain. However, most tobacco users experience nicotine in the oral cavity, and how this oral cavity experience impacts nicotine consumption is relatively unknown. In these experiments, we tested the ingestive and aversive reactions to oral nicotine in rats. Male and female rats (n = 6-10) were implanted with intraoral catheters, allowing for the infusion of liquids directly into the oral cavity without approach or other motivated behaviors. In separate testing sessions, rats received ten infusions of nicotine (each infusion was delivered as 0.2 ml over 4-s) across a range of doses (0, 1, 3, 10, 30 and 100 mg/L nicotine), with 1 – 3 minutes between each infusion. Testing sessions were videotaped and the taste reactivity behavior, a method for assessing responses to gustatory stimuli, was analyzed. Ingestive (rhythmic mouth movements, tongue protrusions, and lateral tongue movements) and aversive (gapes, head shakes, and forelimb flails) responses were scored for the 6-s following each infusion. Lower doses of nicotine (1 mg/L in females and 3 mg/L in males) produced significant increases in ingestive responses compared to water, whereas higher doses (10 mg/L and above in females, and 30 mg/L in males) resulted in significant increases aversive taste reactions. These results suggest that intraoral nicotine is perceived as both reinforcing and aversive, dependent on the dose, and that females are more sensitive to intraoral nicotine. This property of nicotine could contribute to nicotine consumption and the abuse liability of tobacco products. Experiments in progress are testing the receptor subtypes in the oral cavity mediating these separate behavioral responses to nicotine.

P45

Oro-Sensory Neural Processing During Distraction

I DUIF[1], J WEGMAN[1], M MARS[2], K DE GRAAF[2], PAM SMEETS[2], E AARTS[1]

[1]Radboud University, Nijmegen, Netherlands, [2]Wageningen University, Wageningen, Netherlands

Distracted eating is associated with increased food intake. However, the underlying neural mechanisms are unknown. Processing in taste-related brain regions (e.g. insula and orbitofrontal cortex (OFC)) could potentially be attenuated by distraction, causing increased food intake.To test this, 46 healthy, normal weight subjects underwent two fMRI sessions while performing a visual detection task varying in attentional load (high or low distraction). During the task, subjects received sips of a high or low sweet isocaloric drink to assess taste processing. In addition, we measured differences in blood glucose levels and ad libitum food intake of chocolate sweets between the low and high distraction session.We found marginally lower blood glucose increases on the high versus low distraction session (2.5 ± 0.2 (high) vs. 2.9 ± 0.2 (low) Δmmol/L, $p = .068$). Moreover, subjects ate more on the high (versus low) distraction day, but only when the high distraction day was second (77.1 ± 9.2 (high) vs. 64.3 ± 8.2 (low) g., $p = .019$). Finally, we assessed effects of distraction on activation of OFC and insula regions-of-interest (determined with high>low sweetness contrast). We did not find an interaction effect between distraction and sweetness in these ROIs. However, when taking individual differences in glucose increase into account, tentative results show a relation between taste activation in the OFC and glucose increases during high versus low distraction ($r = -.359$, $p = .029$). This suggests that distraction alters the link between OFC processing and blood glucose levels.

P46

Pleasant Taste Anticipation And Processing In Overweight And Obese Individuals Compared To Normal-Weight People: An Event-Related Potential Study

IS HENSELS, D TALMI, S BAINES

Division of Neuroscience and Experimental Psychology, University of Manchester, Manchester, United Kingdom

The incentive sensitisation theory, as applied to obesity, poses that obesity is partly caused by hyper-reactivity to food cues, combined with blunted reward responses to food consumption. This study is the first to test this hypothesis using EEG. Normal-weight (NW; N=27; BMI=18.5-24.9) and overweight/obese participants (OW; N=19; BMI≥25) were conditioned to associate geometric shapes with pleasant or neutral tastes, and ERPs in response to the shape and taste delivery were measured. On each trial, participants rated the pleasantness and intensity of the taste on a scale from 1 to 9 (9=most pleasant/intense). Squash (with concentration tailored to the participant) was used as the pleasant taste; the neutral taste was distilled water with 2 mM $NaHCO_3$ and 15 mM KCl. Data were preprocessed in SPM and analysed in SPSS using ANOVAs and t-tests. There were no differences in neural response to the shapes between the two groups, suggesting no difference in anticipation. For the taste, there was a valence by weight interaction on N2 amplitude (325-400ms). N2 amplitude to the pleasant taste was smaller for OW (M=0.53 μV, SD=1.72) than NW (M=-1.46 μV, SD=4.56; t(35)=2.06, p=.046, equal variances not assumed). This may indicate less attention to pleasant tastes in OW. There was no such difference for neutral taste. The behavioural data also showed decreased pleasantness and intensity ratings of pleasant tastes in OW (M=5.56, SD=0.95 and M=5.22, SD=1.25 respectively) compared to NW (M=6.16, SD=0.84 and M=5.94, SD=1.12 respectively; t(44)=2.28, p=.027 and t(44)=2.04, p=.048 respectively). This study shows blunted neural and behavioural responses to pleasant tastes in OW, thereby uniquely contributing to the field of taste processing and obesity.

P47

Effect Of Taste Manipulation On Food Cue-Elicited Craving & Subsequent Intake Of Palatable Food

LJ GERMEROTH[1], AN PIZZUTO[2], JK PABLA[2], MD LEVINE[1]

[1]University of Pittsburgh Medical Center, Pittsburgh, PA, United States, [2]University of Pittsburgh, Pittsburgh, PA, United States

Food cue-reactivity tasks have been used to induce and evaluate food cravings. The present study examined taste manipulation during a food cue-reactivity task to optimize cue-elicited craving responses and predict food intake. Participants with overweight/obesity (n=35; *M* age=33.46 years [*SD*=13.27]; *M* BMI=32.91 kg/m^2 [*SD*=5.34]) engaged in one lab session during which they were randomized to a 'No Taste' or 'Taste' condition. Participants in both conditions reported baseline food craving and observed low-calorie (LC) and high-calorie (HC) photographic and in vivo food cues during a cue-reactivity task. The Taste group tasted in vivo food cues and the No Taste group did not. Cue-elicited craving was assessed after

each cue. Total food intake of palatable foods was measured during a 10-min bogus taste task. Height and weight were collected. Mixed effect models assessed effects of condition/group (No Taste, Taste), cue type (LC, HC) and cue mode (photographic, in vivo) on cue-elicited craving, adjusting for baseline craving. A *t*-test evaluated the effect of condition on subsequent intake. Results indicated main effects of cue type ($p< .0001$) and mode ($p=.003$) on cue-elicited craving, such that cue-elicited craving was higher for HC vs. LC cues and for in vivo vs. photographic cues. Significant group X cue type ($p=.007$) and group X cue mode ($p=.009$) interactions indicated that both groups had higher cue-elicited craving to HC vs. LC cues, and that cue-elicited craving was higher for in vivo vs. photographic cues for the No Taste group only. Food intake was higher in the Taste vs. No Taste group ($p< .0001$). These findings suggest that incorporating taste into food cue-reactivity tasks does not optimize cue-elicited craving, but does heighten subsequent palatable food intake.

P48 **Spice It Up! Results Of A School-Based Intervention To Increase Vegetable Intake Among Rural Adolescents**

JR FRITTS[1], M BERMUDEZ[2], RL HARGROVE[2], L ALLA[2], C FORT[2], Q LIANG[2], T CRAVENER[2], BJ ROLLS[2], CR D'ADAMO[3], JE HAYES[1], KL KELLER[2]

[1]Department of Food Science, The Pennsylvania State University, State College, PA, United States, [2]Department of Nutritional Sciences, The Pennsylvania State University, State College, PA, United States, [3]Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, MD, United States, [4]Department of Family and Community Medicine, University of Maryland School of Medicine, Baltimore, MD, United States

Adolescents do not consume enough vegetables, thus novel approaches to increase intake within school lunch programs are needed. In phase I of this 2-part study, we hypothesized that adding herbs and spices to common vegetables would increase students' intake compared to when served plain (with oil and salt alone). Over 32 sessions in the school cafeteria, student intake and "choice to eat again" were compared for 8 seasoned and 8 plain vegetable recipes. Intake was assessed by measuring plate waste and student reported "choice to eat again." Two-way ANOVAs testing the effect of condition (plain, seasoned) and age group (middle, high school) found that middle schoolers (11-14 yr) ate more plain than seasoned broccoli (P=0.03), cauliflower (P=0.04) and corn and peas (P< 0.0001). High schoolers (14-18 yr) ate more plain than seasoned green beans (P=0.02) but showed a trend toward higher intake of seasoned black beans and corn (P=0.065). High schoolers also consumed more seasoned vegetables than middle schoolers. A Mantel-Haenszel test found that more students said they would eat five of the vegetables again when they were plain than when seasoned. In phase II, we tested the impact of 5 repeated exposures to 2 seasoning blends (dill and Latin) served on a variety of vegetables during school lunch, on intake and choice to eat again outcomes. Post-exposure, we saw a trend toward higher intake of seasoned broccoli (P = 0.07) and increased percentage of students reporting they would eat seasoned broccoli again (77.9 to 91.5% for middle school, 86.2 to 96.2% for high school, P=0.003). No exposure effects were seen for black beans and corn. These studies show that while younger students may initially favor plain vegetables, seasonings could boost intake long term.

P49 **Links Between Oxytocin And Binge Eating Are Mediated By Addictive Personality Traits And Preference For Sugar And Fat: A Multilocus Genetic Profile (Mlgp) Paradigm**

C DAVIS
York University, Toronto, ON, Canada

Oxytocin is an evolutionarily-ancient neuropeptide that aids in the regulation of many survival behaviors including affiliation, reproduction, and food intake. Hypothalamic oxytocin neurons send projections throughout the central nervous system, including to the mesocorticolimbic dopamine system where they have an enriched presence, and contribute importantly to the regulation of rewarding behaviors. This is the first study to investigate genetic markers of oxytocin availability in relation to *binge eating*. Snce individual polymorhic loci typically contribute only a small proportion of phenotypic variance, we used a quantitative index whereby genetic variants are aggregated to reflect numerically a polygenic characteristic. In a previous study, 4 single nucleotide polymorphisms (SNPs) on the Oxytocin Receptor gene [*OXTR*] and 2 on the Cluster-of-Differentiation 38 [*CD38*] gene - the latter of which influences the release of oxytocin - were significantly related to measures of *reward sensitivity* and were thereby combined to create a MLGP score. Community-recruited healthy adults (n=426) took part in the study. Results indicated that the MLGP had a significant direct link with binge eating, and an indirect effect via addictive personality traits and a preference for sugar and fat (all p-values < 0.05). Findings confirm the important role of oxytocin availability in food preferences and the motivational traits that contribute to addictive tendencies towards calorie-dense foods.

P50 **Impact Of Repeated Caffeine Administration On Bitter Taste Detection, Suprathresholds, Beverage Properties, And Salivary Proteins In Adolescents**

JL TEMPLE, J DROZDOWSKY, E ISENHART, RN MALIK, K KAY, AM TORREGROSSA
University at Buffalo, Buffalo, NY, United States

Caffeine is a common food additive that is extremely bitter. As adolescents transition to adulthood, they increase consumption of highly caffeinated beverages, such as energy drinks or coffee. Understanding the mechanisms that underlie changes in bitter acceptance may provide insight into why

beverage consumption patterns change across development. We hypothesized that 1) repeated caffeine consumption would increase liking and decrease bitterness ratings of beverages relative to a placebo and 2) repeated caffeine intake would increase bitter detection thresholds, decrease suprathreshold ratings, and change salivary protein expression. Twenty-eight adolescents (12 – 15 y) had detection thresholds and suprathreshold ratings for caffeine measured and were randomized to consume a novel-flavored beverage with added water (n=7), quinine (n = 10; 0.02mg/kg), or caffeine (n=11; 2 mg/kg) every day for a week. After 7 days of daily consumption, caffeine detection thresholds and suprathresholds were reassessed. There was a trend toward a main effect of group on change in detection thresholds from baseline to post-intake ($F(2, 25) = 3.2$; $p = 0.058$), with the water group showing a significant decrease in detection threshold relative to the other groups. There was a main effect of group on suprathreshold ratings for the highest concentration of caffeine ($F(2, 26) = 4.6$; $p = 0.02$) with the water group increasing bitterness ratings and the other groups showing no change. Finally, here was a significant interaction of group and sex over time for beverage liking ($F(8, 38) = 2.3$; $p = 0.042$) and bitterness ($F(8, 38) = 2.2$; $p = 0.06$) with effects in females and not males. Future aspects of this study will measure the salivary proteins that accompany these changes.

P51 **Virtual Portion Size Selection Task, Under Momentary And Recalled Stress Predicts Snack Intake In A Stressful Laboratory Eating Session**

JD HAMM[1], RR KLATZKIN[3], S TAMURA[1], J BRUNSTROM[2], M HERZOG[1], M MA[1], HR KISSILEFF[1]

[1]Columbia University Medical Center, New York, NY, United States, [2]University of Bristol, Bristol, United Kingdom, [3]Rhodes College, Memphis, TN, United States

Virtual portion size selection tasks (VPST) have been used as proxy measures for food intake in healthy and eating-disordered individuals. The ability of VPST to predict intake under stressful conditions has not been tested. The hypothesis was that portions selected under both a recalled interpersonal stress and a momentary ("how much would you eat right now") task can predict actual snack intake. VPST for high-, and low-, energy-dense, crossed with sweet and non-sweet, snack foods (potato chips, apples, olives, chocolate, caramel popcorn, pretzels) were given to 21 women (age = 19.3 Yr +/- .27 SE, BMI = 23.8 kg/M^2 +/ 1.6 SE) during a screening trial for recalled stress, and before snacks (potato chips, M&M's, Oreos) for momentary task, eaten after either a 20-min stressor (Trier Social Stress Test), or rest, trial. *After the stressor*, but not *after rest*, milk chocolate (Hershey's Kisses) portion for recalled stress predicted momentary portion size ($\varrho = 0.498$, $p = 0.042$) for milk chocolate, and for actual intake of M&Ms intake ($\varrho = 0.647$, $p = 0.005$) . Momentary portion size of chocolate predicted actual amount eaten for M&M's *after stress* ($\varrho = 0.624$, $p = 0.002$), but not *after rest* ($\varrho = 0.045$, $p = 0.845$) . Conversely, *after rest*, but not *after stress*, typical portion size of milk chocolate predicted momentary portion size ($\varrho = 0.907$, $p = 0.00002$) but did not reach statistical significance for actual intake of M&M's ($\varrho = 0.490$, $p = 0.089$). Momentary portion size of chocolate did not predict M&M intake *after rest* ($\varrho = 0.045$, $p = 0.845$). Portion size selections during actual and recalled stress are both food- and context-specific and could serve as proxy measures of stress-induced eating, in both research and clinical settings.

P52 **Roux-En-Y-Gastric Bypass (Rygb) Surgery Enhances The Metabolic Capacity Of Enterocytes From High Fat Diet-Fed Rats**

S KAUFMAN, D RAMACHANDRAN, N WEISSFELD, W LANGHANS, M ARNOLD
Physiology and Behavior Laboratory, ETH Zurich, Schwerzenbach, Switzerland

RYGB is still the most effective treatment of obesity and its comorbidities, but the signaling mechanisms that mediate the beneficial effects of RYGB are largely unknown. Results from RYGB rodent models as well as human patients suggest that some of the improvements are due to functional and morphological changes in the small intestine. We therefore investigated the metabolic flux of primary enterocytes, isolated from the jejunum of high fat diet (HFD) fed rats one month after RYGB or sham surgery. Using the Seahorse extracellular flux analyzer (XF96), we measured enterocyte oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) immediately after isolation. Enterocytes isolated from RYGB rats showed a "healthier" response to a so-called mitochondrial stress test, a method to measure basal respiration, ATP-linked respiration, proton leak, maximal respiration and non-mitochondrial respiration. Especially in the presence of stressor compounds (such as oligomycin), OCR of RYGB cells remained higher than OCR of sham cells in response to the inhibition of the ATP synthase. This indicates that RYGB enhances the metabolic capacity of enterocytes exposed to HFD. We found no differences between primary enterocytes of HFD-fed RYGB rats and healthy chow-fed rats. Whether the

healthy metabolic profile of RYGB enterocytes is cause or consequence of the reported reduction in body weight and improvement of the various comorbidities requires further investigation.

P53

Mechanisms Underlying The E Cacy Of A Rodent Model Of Vertical Sleeve Gastrectomy &Ndash; A Focus On Energy Expenditure

BJ OLDFIELD, CC LEE, A STEFANIDIS
Monash University, Melbourne, Australia

Bariatric surgery remains the only effective treatment for morbid obesity and Vertical Sleeve Gastrectomy (VSG) is the most widely performed of these surgeries. VSG is associated with reduced appetite, however, the contribution of reduced energy expenditure in brown adipose tissue (BAT) to VSG-induced weight loss, remains unclear. Diet-induced obese male Sprague-Dawley rats (n=35) underwent VSG, sham-operation or pair feeding to the food consumed by the VSG group. Rats were also implanted with biotelemetry devices to assess BAT temperature as a measure of thermogenic activity. Food intake, body weight and changes in body composition were assessed. A separate cohort of chow-fed rats (n=33) underwent excision of BAT or chemical denervation (6-OHDA). Fos protein expression was also evaluated in the nucleus of the solitary tract (NTS) in rats (n=20) in response to VSG following intragastric infusion of either water or a mixed meal (Ensure). VSG caused reductions in food intake, body weight ($P< 0.0001$) and fat mass ($P< 0.05$) as well as an increase in BAT thermogenesis($P< 0.05$) and UCP1 expression ($P< 0.01$). There was also beiging of white fat, shown by elevated Cited1 mRNA ($P< .01$) expression in inguinal white fat. The effect of VSG on weight loss and fat mass was significantly reduced in animals with disrupted iBAT function with either method. Intragastric infusion of water in rats with VSG produced an elevation in the number of Fos-labelled neurons in the NTS whereas infusion of the same volume of a mixed-meal (Ensure) resulted in twice as many Fos-labelled neurons in the NTS. These data support a role for BAT thermogenesis in VSG-mediated weight loss. In addition, both stretch and nutrients are likely to contribute to recruitment of brainstem neural relays following VSG.

P54

Roux-En-Y Gastric Bypass Lowers Sucrose Consumption And Preference In Two-Bottle Intake Tests Without Decreasing Concentration-Dependent Licking In A Brief Access Test In Female Rats.

K.M. HYDE[1], G.D. BLONDE[1], C.W. LE ROUX[2], A.C. SPECTOR[1]

[1]Department of Psychology and Program in Neuroscience, Florida State University, Tallahassee, FL, United States, [2]Diabetes Complications Research Centre, Conway Institute, School of Medicine, University College Dublin, Dublin, Ireland

Evidence suggests that decreases in sucrose intake and preference in long-term tests following Roux-en-Y gastric bypass (RYGB) in male rats is unaccompanied by surgically-induced changes in the reinforcing properties of the sugar. Here, we tested whether long-term exposure to sucrose affects concentration-dependent licking to the sugar in brief access tests in female rats. RYGB (n=10) and SHAM (n=12) rats were allowed daily 23-h home-cage access to 0.3 M sucrose in five 46-h two-bottle intake tests (TBTs) across 10 days. Despite a difference in 0.3 M sucrose intake between the groups, preference for the sugar did not significantly differ. When sucrose concentration was increased to 1.0 M for a second 10-day series of TBTs, RYGB animals maintained lower sucrose intake and progressively decreased preference for sucrose compared to SHAM animals. Additionally, three sets of 30-min brief access tests (0.01-1.0 M sucrose, 10-s trials) were given to nondeprived animals before exposure to 0.3 M sucrose, after exposure to 0.3 M sucrose, and after exposure to 1.0 M sucrose. Despite significant changes in home-cage responding to sucrose, surgery did not significantly decrease concentration-dependent licking to sucrose relative to SHAM rats during any of the three sets of brief access tests. In the first set of brief access tests, the number of trials initiated by the RYGB group was actually significantly greater compared with SHAM rats, but the two groups did not differ on this measure of appetitive behavior in the subsequent brief access tests. Similar to findings in male rats, these results suggest that after RYGB, lower sucrose intake and preference in female rats are not likely due to a decrease in the motivational potency of the orosensory properties of the sugar.

P55

Roux-N-Y Gastric Bypass Induces Rapid Neuronal Cell Damage And Inflammation In Nodose Ganglion In Rats

DM MINAYA[1], A TURLEJ[1], SC FARUQUE[1], V LACMANOVIC[1], A HAJNAL[2], PM DILORENZO[3], K CZAJA[1]

[1]Dept. of Veterinary Biosciences & Diagnostic Imaging, Univ. of Georgia, Athens, GA, United States, [2]Dept. of Neural and Behavioral Sciences, The Pennsylvania State University, College of Medicine, Hershey, PA, United States, [3]Dept. of Psychology, Binghamton Univ., Binghamton, NY, United States

Obesity is a leading cause of morbidity and mortality worldwide. Roux-n-Y gastric bypass (RYGB) is the most effective weight loss treatment. However, its effects on the gut-brain vagal connection are largely unknown. In this study, we investigated the short-term (24h) effects of RYGB on plasticity of vagal afferents in the nodose ganglia (NG) and Nucleus Tractus Solitarius (NTS) in high fat fed rats. Male Sprague-Dawley rats consumed a 45% fat diet for two weeks and then subjected to RYGB or sham surgery. 24h later, animals were sacrificed and tissues collected. Neuronal cell damage was determined by TUNEL assay. Inflammation was determined by quantifying the fluorescent staining against the ionizing

calcium adapter binding molecule 1 (IBA 1). Reorganization of vagal afferents was evaluated by fluorescent staining against Isolectin 4 (IB4). Results of the study revealed that RYGB induced neuronal damage and increased inflammation in the NG. In addition, RYGB significantly decreased the density of vagal afferents projecting to the NTS. We did not observe an inflammatory response in the NTS. The observed changes in vagal presynaptic projections to the NTS may affect the altered taste signaling reported after RYGB.

P56 **Roux-En-Y Gastric Bypass Surgery (Rygb) Modulates The Intestinal Lymph Lipid Profile In Rats**

S KAUFMAN[1], W LANGHANS[1], M ARNOLD[1], JP KRIEGER[2]

[1]ETH Zurich, Zurich, Switzerland, [2]University of Zurich, Zurich, Switzerland

RYGB is associated with multiple metabolic improvements, including reduced plasma lipid levels. Whether physiological changes in intestinal lipid absorption and handling contribute to these improvements is, however, still unclear. Therefore, we investigated how the lipid composition of intestinal lymph, as readout of intestinal absorption and handling, is changed after RYGB. We cannulated the mesenteric lymph duct of diet-induced obese, insulin-resistant RYGB or Sham-operated Sprague-Dawley rats and collected lymph samples in relation to spontaneous meals (prior to and 21 days after surgery). We detected 183 lipid species by mass spectrometry and analyzed their abundance by multivariate exploratory methods. First, with principal component analysis and clustering, the lymphatic lipid profile of the RYGB rats was clearly distinct from that of Sham rats 21 days after surgery, indicating that RYGB drastically changes intestinal lymph lipid composition. Second, with volcano plot and partial least squares analysis, we identified 65 lipid species whose abundance was significantly different between RYGB and Sham. Notably, di- and triglycerides were mostly decreased after RYGB, presumably reflecting the reduced food intake. Some lipids, however, were increased in intestinal lymph after RYGB: specifically, we found strong positive correlations between number of carbons, number of double-bonds and fold-change after RYGB. Our results indicate that RYGB modifies intestinal lipid absorption and handling and that enterocytes of RYGB rats release overall less di- and triglycerides, but more of the long-chain, unsaturated lipids into the lymph than Sham rats. Whether these changes lead to the reported improvements in lipid profile and cardiovascular risk requires further investigation.

P57 **Hypothalamic Changes In Offspring Born Of Females Post-Vertical Sleeve Gastrectomy**

RA SPANN, CA ZAMARRIPA, BE GRAYSON
University of Mississippi Medical Center, Jackson, MS, United States

Bariatric surgery has a positive effect on fertility in women in addition to effectively treating obesity and type 2 diabetes. Despite improvement in maternal health, complications can occur in children. Offspring of mothers who have had bariatric surgery can be born small-for-gestational age and are consequently at a much greater risk of obesity as adults. The etiology of this relationship remains unknown. We have previously shown in a maternal rat model of vertical sleeve gastrectomy (VSG) greater permeability of the placental barrier, elevated inflammatory signaling, and higher incidence of apoptosis in the placenta. In the present study, we investigate outcomes in postnatal day 22 pups, measuring molecular and cellular changes in the hypothalamus. Here there is an increase in hypothalamic interleukin 1 beta mRNA expression in pups born to VSG dams when compared to pups from sham operated dams. Immunohistochemical detection of IBA1 positive microglia in the paraventricular nucleus of the hypothalamus shows reduced staining density in VSG pups with no impact on astrocyte density as measured by glial fibrillation acid protein in comparison to pups from sham dams. We have also previously demonstrated greater levels of circulating glucagon like peptide 1 (GLP1) during gestation in VSG dams. Here we show increased expression of GLP1 receptor mRNA in the hypothalamus of VSG pups when compared to Sham pups. These results show that maternal VSG has effects on both the central immune health and hormone responses of offspring postnatally. Future work will determine if these changes are responsible for impaired metabolic control and weight gain.

P58 **Rygb Surgery Induces Subject-Specific Changes Intestinal Fungal Microbiota In Morbidly Obese Patients**

RE STEINERT[1], FHJ SCHUREN[2], V AGAMEMNONE[2], D GERO[1], S TZAFOS[1], H HOSA[1], D VETTER[1], B MISSELWITZ[3], M BUETER[1]

[1]Department of Surgery, Division of Visceral and Transplantation Surgery, University Hospital Zürich, Zurich, Switzerland, [2]Microbiology and Systems Biology, The Netherlands Organization for Applied Scientific Research (TNO), Zeist, Netherlands, [3]Clinic of Gastroenterology and Hepatology, University Hospital Zurich, Zurich, Switzerland

Bariatric surgery, including Roux-en-Y gastric bypass (RYGB), remains the most effective treatment for morbidly obese patients to lower body weight and improve glycemic control. Several interrelated mechanisms have been suggested for this unparalleled efficacy including alterations in the secretion of gastrointestinal hormones, increased delivery of bile acids to distal L-cells, and more recently changes in the composition of the gut microbiota. While changes in bacterial microbiota have been investigated thoroughly, with reported bacterial dysbiosis in the obese and improvement thereof after surgery, changes in the fungal components of the gut microbiota remain unexplored. We used an Internal Transcribed Spacer (ITS)-1 based barcoding approach to characterize fungal diversity in fecal samples of 16 morbidly obese patients before (BMI, 41.6 ± 0.3) and 3 months after RYGB surgery (BMI, 33.9 ± 0.3, $p < 0.001$). We also determined the bacterial microbiota and performed a correlation analysis of altered inter-kingdom relations, and body weight as well as metabolic markers (HOMA, cholesterol, blood pressure). We found that while there are population-

specific changes in bacterial composition in line with previous reports, changes in fungal microbiota were observed only within-subjects, but not on a cohort-level, due to large individual differences in the directions of change. While there were inter-kingdom correlations, we did not detect any correlation between fungal microbiota and improvements in metabolic markers. Our data suggest that the fungal microbiota may not play a causal role in the beneficial effects of bariatric surgery as seen after 3 months. More comprehensive investigations with larger cohorts and over longer periods are required to further prove this hypothesis

P59 **Central Inputs To Preproglucagon (Ppg) Neurons Revealed With A Cre-Conditional Pseudorabies Virus (Prv)**

MK HOLT[1], LE POMERANZ[2], L RINAMAN[1]

[1]Department of Psychology & Program in Neuroscience, Florida State University, Tallahassee, FL, United States, [2]Laboratory of Molecular Genetics, Howard Hughes Medical Institute, Rockefeller University, New York, NY, United States

Glucagon-like peptide-1 (GLP-1) is an anorexic neuropeptide predominately expressed in PPG neurons in the caudal nucleus of the solitary tract (cNTS). Central inputs to the cNTS have been described, but little is known regarding circuits specifically impinging on PPG neurons. Here, we identify circuits upstream of cNTS PPG neurons using a Cre-dependent neurotropic virus, PRV-Introvert-GFP, which replicates and expresses GFP in a Cre-dependent manner. After initial infection of Cre-expressing PPG neurons, GFP expression and retrograde polysynaptic transport are enabled through a single recombination event to reveal input circuits specific to cNTS PPG neurons. PRV-Introvert-GFP (500 nl) was injected bilaterally into the cNTS in transgenic PPG-Cre mice. After 5-9 days, mice were perfused with fixative, and tissue sections processed to localize GFP. GFP-positive neurons were present in multiple CNS regions known to innervate the cNTS, including the spinal cord dorsal horn, reticular formation, area postrema, supratrigeminal nucleus, periaqueductal gray, parasubthalamic nucleus, hypothalamus, bed nucleus of stria terminalis, amygdala, medial prefrontal cortex, and perirhinal cortex. GFP labeling also revealed 2nd- or higher-order projections from areas lacking direct input to the cNTS, including the paraventricular thalamus and hippocampus. Ongoing work will establish the temporal sequence of transsynaptic viral infection within these higher-order regions. These novel anatomical tracing data reveal a structural basis for widespread CNS regulation of hindbrain PPG/GLP-1 neurons that inhibit food intake and other reward-driven behaviors, especially during times of stress.

P60 **Glp-1 Neurons Form A Local Synaptic Circuit Within The Nucleus Of The Solitary Tract**

JP CARD[1,3], AL JOHNSON[1], IJ LLEWELLYN-SMITH[2], H ZHENG[3], R ANAND[4], DI BRIERLEY[4], S TRAPP[4], L RINAMAN[3]

[1]Univ. Pittsburgh, Pittsburgh, PA, United States, [2]Flinders Univ., Bedford Park, SA, Australia, [3]Florida State Univ., Tallahassee, FL, United States, [4]Univ. Coll. London, London, United Kingdom

Glutamatergic neurons that express pre-proglucagon (PPG) and are immunopositive for GLP-1 are sequestered within the caudal nucleus of the solitary tract (cNST) and medullary reticular formation in rats and mice. GLP-1 neurons give rise to an extensive central network in which GLP-1 receptor (R) signaling suppresses food intake, attenuates the reinforcing properties of rewarding stimuli, increases avoidance, and stimulates physiological stress responses. Some of these effects depend on local GLP-1R signaling within the cNST. Previous reports in mice indicate that noradrenergic (A2) cNST neurons express GLP-1R, whereas PPG neurons do not. In the present study, confocal microscopy in rats confirmed that the dendrites of prolactin-releasing peptide (PrRP)+ A2 neurons are closely apposed by GLP-1+ axonal varicosities. Surprisingly, close GLP-1+ appositions also were observed onto the dendrites of PPG/GLP-1 neurons in both rats and mice, and electron microscopy revealed that GLP-1+ boutons form asymmetric synaptic contacts with GLP-1+ dendrites in rats. However, RNAscope confirmed that GLP-1 neurons do not express mRNA for GLP-1R in rats. Similarly, Ca^{2+} imaging of somatic and dendritic responses in mouse *ex vivo* brainstem slices confirmed that identified PPG neurons do not respond directly to synthetic GLP-1, and a cross-breeding strategy revealed that fewer than 1% of PPG-expressing neurons co-express GLP-1R. Collectively, these data reveal a local "feed-forward" synaptic network among GLP-1 neurons that apparently does not utilize GLP-1R signaling. Instead, the network may use glutamatergic receptors to facilitate dynamic recruitment of GLP-1 neural populations that mediate widespread behavioral and physiological responses to internal and external challenges.

P61 **Neurotrophin-4 Is Essential For Survival Of A Large Proportion Of Vagal Afferents That Innervate The Small Intestinal Mucosa**

HK SERLIN, EA FOX
Purdue University, West Lafayette, IN, United States

Vagal afferents that supply the small intestine play a key role in regulating satiation and gastrointestinal (GI) function. We previously showed that neurotrophin-4 (NT-4) is essential for survival of vagal mechanoreceptors that innervate intestinal, but not stomach, myenteric ganglia and contribute to satiation (Fox J Neurosci,2001). Here we use Nav1.8Cre-tdTomato (Nav-Tom) transgenic mice to label these afferents (Gautron JCN,2011;Serlin SSIB,2017) and bred them to NT-4 KO (-/-) mice to investigate the effects of NT-4 loss on vagal intestinal mucosal afferents. Immunohistochemical staining of Tomato was used to label axons and terminals in villi and adjacent to crypts in the proximal duodenum. These neuronal processes were quantified in NT-4-/-;Nav-Tom, NT-4+/-; Nav-Tom and Nav-Tom mice. NT-4-/- mice had a 60% loss of axons entering a villus and 40% loss of

terminal branches at villus mid-height compared to NT-4+/- ($t = 5.23$, $t = 4.05$, respectively; both $p < .05$) and Nav-Tom ($t = 5.83$, $t = 2.77$, respectively; both $p < .05$) mice. There was no difference between NT-4+/- and Nav-Tom mice on either measure ($t = .57$, $p > .05$, $t = .89$, $p > .05$). Vagal crypt afferents, currently being counted, appeared to have a similar loss. These preliminary results suggest a large proportion of vagal mucosal afferents depend on NT-4 for survival. Loss of vagal afferents to small intestine muscle and mucosa, involving both mechano- and chemoreceptors, in NT-4-/- mice supports the organ-specific model of neurotrophin regulation (Brady J Neurosci,1999). It also suggests this mouse model can be used to selectively eliminate vagal afferent innervation of the small intestine without large disruptions to physiology or vagal efferents to study the effects on GI physiology and feeding behavior.

P62

Selective Activation Of Dorsal Vagal Complex Y2-Receptors Increases Food Intake By Rats.

N HUSTON, Z TAYLOR, S GOTTLIEB, S APPLEYARD, RC RITTER
Department of Integrative Physiology and Neuroscience, Washington State University, Pullman, WA, United States

Previously we reported that injections of PYY 3-36, an NPY Y2-receptor (Y2R) agonist, into the rat dorsal vagal complex (DVC) increased food intake. To determine whether PYY 3-36-induced food intake is mediated by selective DVC Y2R activation we employed DVC-localized 100 nl injections of selective Y1R, Y2R and Y5R agonists and antagonists. DVC injections of PYY 3-36 (25, 50 and 125 pmols) significantly increased food intake between 30 and 240 min post injection (n=8-10). The Y1R agonist, Leu^{31}, Pro^{34}, NPY, did not increase food intake at any dose (n=8). However, the Y5R agonist, [cPP^{1-7}, NPY^{19-23}, Ala^{31}, Aib^{32}, Gln^{34}] - hpancreatic polypeptide (50 pmols), did increase food intake (n= 6). Increased food intake in response to PYY 3-36 was prevented by injection of the Y2R antagonist BIEE 0246 (n=6), but not by the Y5R antagonist NPY 5RA972 (n=6). Moreover, increased food intake following DVC injection of Y5R agonist was prevented by injection of the Y2R antagonist, BIEE 0246 (n=9). We conclude that Y2R activation is necessary and sufficient to increase food intake following YR agonist injections into the dorsal vagal complex. Y2R are expressed by scattered NTS neurons and by approximately 50% of vagal afferent neurons in the nodose ganglia. Reports by others indicate that peripheral Y2R activation reduces food intake, perhaps by exciting vagal afferents. However, electrophysiological studies reveal that presynaptic Y2R inhibit vagal afferent endings in the NTS. Moreover, NTS injection of Y2R agonist prevents reduction of food intake by peripherally injected CCK, an effect mediated by peripheral vagal activation. Our results are consistent with the hypothesis that Y2R activation in the DVC increases food intake by attenuating vagal afferent synaptic function.

P63

Estradiol Decreases Expression Of Genes Associated With The Plc-Ip_3-Pkc Pathway In The Subfornical Organ In Ovariectomized Female Rats

JA HOWELL, C WHORF, J SANTOLLO
Department of Biology, Lexington, KY, United States

We have previously demonstrated that activation of specific estrogen receptor (ER) subtypes has divergent effects on angiotensin II (AngII)-stimulated fluid intake in female rats. Specifically, activation of ERα decreases water intake, whereas activation of ERβ and GPER-1 decrease saline intake. Because AngII stimulates water and saline intake through separate cell signaling pathways in male rats, we hypothesized that ER subtypes selectively decrease water and saline intake through modulation of distinct intracellular pathways. First, we tested whether the cell signaling pathways that control water and saline intake in male rats are similar in female rats. Water and saline intake were measured in two groups of female rats (n=18) after the following intracerebroventricular treatments: DMSO (vehicle)/ TBS (vehicle), 100 μM chelerythrine (PKC inhibitor)/TBS, DMSO/10ng AngII, and 100 μM chelerythrine/10ng AngII or DMSO/TBS, 1 mM U0126 (MAP Kinase inhibitor)/TBS, DMSO/10ng AngII, and 1 mM U0126/10ng AngII. As expected, inhibiting PKC reduced water, but not saline, intake and inhibiting MAPK reduced saline, but not water, intake ($p< 0.05$). Next we identified molecules in these signaling pathways that are modulated by estradiol. Ovariectomized rats (n=8) were treated with 20μg estradiol benzoate (EB) or oil and 48 h later brains were collected and the subfornical organ (SFO), paraventricular nucleus (PVN), and anteroventral region of the third ventricle (AV3V) were dissected. Preliminary data suggests that EB-treatment reduced expression of genes in the PKC pathway in the SFO, but not in the PVN or AV3V. Ongoing studies are examining expression of genes in the MAPK pathway. Future studies will investigate which ER subtype is mediating any changes found in gene expression.

P64 **The Imprecision Of Energy Intake Of Humans To Compensate For Imposed Energetic Errors.**

DA LEVITSKY, Y ZHONG, LK BARRE
Division of Nutritonal Sciences, Cornell University, Ithaca, NY, United States

The fact that the population gains only about one kg a year (1750 kcal) yet consumes about 800,000 kcal a year is frequently quoted as a demonstration of the precision to which humans adjust energy intake to compensate for surfeits or deficits in energy balance. The purpose of this review was to estimate the precision to which energy intake compensates for imposed errors in energy balance. A systematic review of the literature was performed to identify studies where energetic errors were imposed on humans and energy intake measured. The review consisted of eight areas of study: (a) Alternate Day Fasting, (b) Diet Composition, (c) Exercise, (d) Overfeeding, (e) Portion Size, (f) Meal Skipping, (g) Sugar or Fat Substitute and (h) Underfeeding. A total of 197 studies were compiled consisting of 544 groups (12166 participants). The Energetic Error, defined as (Expected Mean Energy Intake – Observed Mean Energy Intake) / Expected Mean Energy Intake, was calculated for each study. The average absolute Energetic Error was 25%. Precise biological regulation of intake, would suggest an average absolute Energetic Error of 0%, These results challenge the view that human food intake is tightly linked to biological mechanisms involved in the regulation of body weight.

P65 **Central Fibroblast Growth Factor 21 (Fgf21) Is Required To Increase Whole Body Energy Expenditure In Mice But Not For Fgf21 Induced Browning Of White Adipose Tissue.**

BN DESAI[1], ML MATHER[1], JS FLIER[1], FM FISHER[1], E MARATOS-FLIER[1,2]

[1]Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston , MA, United States, [2]Novartis Institutes for BioMedical Research (NIBR), Cambridge, MA, United States

Exogenously administered fibroblast growth factor 21 (FGF21) causes weight loss, increases energy expenditure (EE) and induces browning of inguinal white adipose tissue (IWAT) in mice. Furthermore, central administration of FGF21 at doses that lead to sub-threshold concentrations in the periphery also induces browning. However, the relative contribution of FGF21 acting through the central nervous system compared to direct paracrine/autocrine action on adipose tissue is unknown. To dissect the central and peripheral actions of FGF21 on browning and EE, we evaluated the pharmacologic response to FGF21 in mice with a brain specific deletion of β-klotho, the obligate co-receptor of FGF21 (KLB BKO mice). KLB BKO mice and their flox/flox littermates (controls) were infused subcutaneously with either high dose FGF21 (24μg/day) or saline via mini-osmotic pumps for 5 days. In control mice, FGF21 infusion resulted in marked weight loss compared to saline treated counterparts. This was accompanied by an increase in EE. By contrast, KLB BKO mice treated with FGF21 failed to lose weight and were unable to increase EE. FGF21 infusion had no effect on food intake in either group. As expected, FGF21 infusion caused a 10-fold induction of uncoupling protein 1 (UCP1) in IWAT of control mice. Interestingly however, FGF21 infusion also induced IWAT UCP1 8-fold in KLB BKO mice lacking FGF21 action in the brain. Expression of other molecular browning markers CIDEA, Cox7a, Cox8b was also increased in IWAT of both FGF21 treated controls and KLB BKO. These data show that central FGF21 action is required for effects of FGF21 on EE and associated weight loss. In contrast, central FGF21 action is not exclusively required to brown IWAT and may act in combination with direct peripheral actions.

P66 **A Role For Dorsomedial Hypothalamic Neuropeptide Y In Glucoprivation-Induced Feeding And Hyperglycemia**

HZ ZHANG, S BI
Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, United States

Lesions of the dorsomedial hypothalamus (DMH) result in a deficit in feeding response to 2-deoxy-D-glucose (2-DG)-induced glucoprivation, indicating the importance of the DMH in integrating glycemic signal to modulate food intake. However, the neuronal basis of this DMH role has yet to be determined. Data have shown that the DMH contains neuropeptide Y (NPY)-expressing neurons and alterations in DMH NPY signaling affect food intake and hepatic glucose production. These data imply that DMH NPY neurons may act as glucose-sensing neurons to affect food intake and glucose homeostasis. Here, we studied this role using three approaches to manipulate DMH neuronal activity or DMH NPY signaling: 1) activation of DMH neurons by the Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) technology; 2) adeno-associated virus (AAV)-mediated expression of NPY in the DMH; and 3) AAV-mediated RNAi for knockdown of NPY in the DMH. We found that 2-DG-induced glucoprivation promoted *Npy* gene expression in the DMH. Activation of DMH neurons by DREADD ligand, clozapine-N-oxide (CNO), significantly elevated food intake in 2-DG treated group. Overexpression of DMH NPY enhanced 2-DG-induced food intake, whereas knockdown of DMH NPY attenuated 2-DG-induced food intake, suggesting that DMH NPY contributes to 2-DG-induced feeding response. Interestingly, DMH NPY overexpression also attenuated 2-DG-induced hyperglycemia. Determinations of hepatic gene expression revealed that glucose 6-phosphate expression was significantly increased in response to 2-DG, but this increase was reduced in the NPY overexpression group. Together, these findings provide evidence suggesting that DMH NPY neurons sense glycemic signal to modulate food intake and glucose homeostasis.

P67 **Hypothalamic Trpv1-Expressing Neurons And The Regulation Of Energy Homeostasis**

LD DESMOULINS[1], BV HAMLING[2], A KATSURADA[1], A ZSOMBOK[1,2]

[1]Department of Physiology, School of Medicine, Tulane University, New Orleans, LA, United States, [2]Tulane Brain Institute, New Orleans, LA, United States

Transient Receptor Potential Vanilloid type 1 (TRPV1), a nonselective cation channel is associated with the regulation of homeostatic functions and linked to the development and progression of obesity and diabetes mellitus. Moreover, capsaicin, a TRPV1 agonist in high fat diet prevented the development of obesity and improved insulin sensitivity. TRPV1 is expressed in the hypothalamus and our previous studies demonstrated that liver-related hypothalamic neurons are regulated by TRPV1; however, the specific physiological role of TRPV1-expressing ($TRPV1^+$) neurons has not been revealed. In this study, we tested the hypothesis that stimulating $TRPV1^+$ neurons in the lateral and posterior hypothalamus (LH/PH) alters food intake and improves glucose tolerance. Designer receptor exclusively activated by designer drugs (DREADD) approach was used to determine the effect of stimulation and inhibition of $TRPV1^+$ neurons *in vivo*. A single intraperitoneal injection of clozapine-N-oxide (CNO; 1 mg/kg) was used to stimulate or inhibit $TRPV1^+$ neurons in the LH/PH, while metabolic and cardiovascular parameters were evaluated. Stimulation or inhibition of $TRPV1^+$ neurons in the LH/PH did not affect food intake during 6 h of a refeeding test, or glucose tolerance after ip injection of glucose (2 g/kg). Similarly, systolic blood pressure and heart rate were not significantly changed following stimulation or inhibition of $TRPV1^+$ in LH/PH. In addition, the body temperature of mice was not altered following modulation of $TRPV1^+$ neurons in the LH/PH. In summary, our data suggest that $TRPV1^+$ neurons located in the LH/PH are not involved in the central control of energy homeostasis and further studies are needed to reveal the physiological role of TRPV1-expressing neurons in the LH/PH.

P68

Analysis Of Synergism Between Exercise And Trpv1 Activation To Enhance Metabolic Activity

HA TOWNSEND[1], V KRISHNAN[1], E LARSON-MEYER[2], P BASKARAN[1], B THYAGARAJAN[1]

[1]School of Pharmacy University of Wyoming, Laramie, WY, United States, [2]Dept. of Family and Consumer Sciences, Laramie, WY, United States

Obesity results from an imbalance between energy intake and expenditure. Regular exercise and calorie (energy) restriction are considered as effective strategies to prevent obesity. Exercise enhances energy expenditure trough increased movements and stimulation of AMPK. Research from our laboratory suggests that activation of transient receptor potential vanilloid subfamily 1 (TRPV1) by capsaicin activates AMPK, enhances energy expenditure and protects mice from obesity. Since both exercise and TRPV1 activation enhance AMPK, we hypothesize that the synergistic effect of regular exercise (by rigorously training mice on a rotarod for 24 minutes long and 4-days a week) and TRPV1 activation (by feeding oral capsaicin in HFD) will enhance metabolism to abate metabolic dysfunctions. We used wild-type and AMPK kinase-dead (KD; skeletal and cardiac tissue specific) mice that received a HFD (60% kcal) ± Capsaicin (0.01%)]. Weekly weight gain and food/water intake were recorded. We evaluated the expression of TRPV1, AMPK and sirtuin-1 in the gastrocnemius muscle, white and brown fat by qRT-PCR and measured the respiratory quotient and heat production by indirect calorimetry. Our results indicate that the effect of CAP feeding significantly enhanced the performance of the mice on the rotarod, suppressed weight gain without modifying energy intake. We did not find any difference between capsaicin (± exercise) mice group, which suggests a significant effect of CAP to enhance metabolic activity independent of exercise synergism. This translational data is of great significance in combating metabolic disorders in humans and valuable for those who cannot perform exercise due morbid obesity or impairment.

P69

Glucose Sensing Neurons Regulate Glucose Homeostasis By Counter-Balancing Insulin-Producing Cells And Glucagon-Producing Cells

Y OH[1], JS LAI[1], HJ MILLS[1], JG WANG[1], F ABU[1], GSB SUH[1,2]

[1]Skirball Institute of Biomolecular Medicine, Neuroscience Institute, Department of Cell Biology, New York University School of Medicine, New York, NY, United States, [2]Department of Biological Sciences, Korea Advanced Institute of Science and Technology, Deajeon, South Korea

Blood glucose level is detected by glucose sensing neurons in hypothalamus and alpha, beta cells in pancreas and regulated by pancreatic hormones such as insulin and glucagon. Glucose sensing neurons also regulate glucose homeostasis by sending signals to the endocrine pancreas via parasympathetic and sympathetic nervous system. However, although the importance of the role of glucose sensing neurons to maintain glucose homeostasis, the physiological and endocrinological functions of glucose sensing neurons are not fully understood in mammals. Here we show that the novel glucose sensing neurons in *Drosophila* brain which is named *CN* neurons activate insulin-producing cells (IPCs) in the brain and inactivate glucagon-producing cells in corpora cardiaca (CC). *CN* neurons are directly activated by nutritive sugars not by non-nutritive fake sugars. Glucose transporters, KATP channels and voltage dependent calcium channels are involved in the neuronal activation of *CN* neurons. Interestingly, nutrient-dependent plastic changes occur in the two axon branches of *CN* neurons. A signal from *CN* neurons is essential for the insulin secretion on IPCs and required for IPCs to sense glucose. On the other hand, an inhibitory signal from *CN* neurons regulates glucagon secretion on the glucagon-producing cells. Together, we propose that the connections between *CN* neurons and insulin and glucagon-producing cells are essential for maintaining glucose

homeostasis and balanced food choice behavior by counter-balancing the secretion of insulin and glucagon according to the internal energy status of the animals.

P70 **Sirt3 Overexpression In Astrocytes Affects Glucose Metabolism And Energy Homeostasis**

N WEISSFELD, W LANGHANS, A MANSOURI
Physiology and Behavior Laboratory, ETH Zurich, Schwerzenbach, Switzerland

Astrocytes are key players in brain metabolism. Unlike neurons, astrocytes store glycogen and are able to oxidize fatty acids and produce ketone bodies. Astrocyte-derived ketone bodies have been implicated in the control of eating. Sirtuin3 (SIRT3), a ubiquitous mitochondrial NAD^+-dependent deacetylase, deacetylates and activates several enzymes involved in fatty acid oxidation and the TCA cycle. We here tested whether overexpression of SIRT3 in astrocytes affects energy homeostasis and glucose metabolism in mice. Mice with an inducible (CreERT2), astrocyte-specific (GFAP promotor) SIRT3 overexpression (SIRT3ki mice) and their corresponding littermates (control) were fed either a low-fat diet (LFD, 10% energy from fat) or high-fat diet (HFD, 60% energy from fat) for 12 weeks prior to induction of the SIRT3 overexpression by tamoxifen (TAM) injection. We found that both SIRT3ki and control mice ate similar amounts of food with ad-libitum access to LFD (6 weeks) or HFD (12 weeks) after TAM injection, and were similarly prone to body weight gain (on the HFD). On HFD, SIRT3ki mice had lower energy expenditure immediately after the TAM injection and stored 34% more fat, but had a much higher plasma insulin response to an oral glucose tolerance test (OGTT) and greater glucose excursions in an “insulin sensitivity test” (IST) compared to the HFD-fed controls. On the other hand, SIRT3ki mice on LFD displayed similar glucose tolerance (OGTT) as well as glucose excursion (IST) as control mice, but showed a lower respiratory quotient in the light phase immediately after the TAM injection. Overall, SIRT3 overexpression in astrocytes affects glucose metabolism and energy homeostasis. Further studies are required to unravel the mechanisms underlying these effects.

Friday, July 20, 2018

8:30 - 10:30 AM	Calusa ABC
Symposium 4: Gut Hormones as Novel Targets for Addiction Treatment	

Chair(s): Tony Goldstone and Stephanie Fulton

8:30 **Peripheral Hormones Tune Phasic Dopamine Responses Evoked By Nutritive And Drug Rewards**

MF ROITMAN
University of Illinois at Chicago, Chicago, IL, United States

The phasic release of the neurotransmitter dopamine is thought to play a key role in reinforcement and motivational processes. The reinforcing value of stimuli and the goal-directed behavior they trigger depend, in large part, on physiological state (e.g. hunger, satiety). How physiological state is communicated to the mesolimbic dopamine system is only beginning to be elucidated. We have used fast-scan cyclic voltammetry to measure dopamine release, and fiber photometry to measure dopamine cell body activity, in awake and behaving rats and find phasic dopamine is evoked by food, fluid, as well as cues that predict them. Manipulations of physiological state (e.g. hunger, thirst, sodium appetite) modulate these responses. Moreover, peripheral signals known to relate physiological state to the central nervous system are often sufficient to recapitulate the effects of physiological state on phasic dopamine signaling. These results will be discussed before addressing whether some of these peripheral signals may serve as targets for modulating phasic dopamine responses to drugs of abuse (e.g. cocaine). Indeed, we have found that the GLP-1 receptor agonist Exendin-4 suppresses phasic dopamine signaling that would normally be stimulated by intravenous cocaine. Thus, our results suggest that central receptors for 'homoestatic' signals may hold promise for tempering behavior directed at drugs of abuse through modulation of phasic dopamine signaling.

9:00 **Can Glp-1 Receptor Agonists Be Re-Purposed For Cocaine Addiction?**

HD SCHMIDT[1,2]
[1]Dept. of Biobehavioral Health Sciences, University of Pennsylvania, Philadelphia, PA, United States, [2]Dept. of Psychiatry, University of Pennsylvania, Philadelphia, PA, United States

A growing literature indicates that glucagon-like peptide-1 (GLP-1) receptors play an important role in drug-mediated behaviors. Our studies show that activation of central GLP-1 receptors is sufficient to attenuate voluntary cocaine taking and seeking in rats. Specifically, we identify behaviorally selective doses of a GLP-1 receptor agonist that reduce cocaine reinforcement and the reinstatement of cocaine seeking, an animal model of relapse, and do not produce adverse malaise-like effects nor affect food intake in cocaine-experienced rats. We also show that cocaine activates GLP-1-expressing neurons and increases expression of preproglucagon (PPG) in the nucleus tractus solitarius (NTS). Together, these results suggests that increased central GLP-1 signaling may represent a homeostatic compensatory response to cocaine taking that serves to reduce further drug consumption. Interestingly, abstinence following cocaine self-administration is associated with decreased expression of PPG in the NTS, which may function to facilitate drug seeking during withdrawal. Collectively, these findings indicate that cocaine dynamically alters expression of endogenous central PPG expression and identify a novel GLP-1-mediated neuroendocrine mechanism underlying cocaine taking and seeking. These preclinical findings provide strong rationale for pilot clinical trials of GLP-1 receptor agonists in human cocaine.

9:30 **Effects Of Ghrelin, Glp-1 And Amylin On Alcohol And Drug Reward**

E JERLHAG
Department of Pharmacology, Institute of Neuroscience and Physiology, The Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden

Alcohol dependence causes severe health problems for individuals and is a major cost to society. The number of available medications is limited and there is therefore a substantial need for new pharmacological interventions. It is thus of utterly importance to understand the neurochemical mechanisms underlying development of alcohol addiction. Recent studies have shown that appetite regulatory peptides may be important modulators

thereof. Indeed, our initial studies display that central administration of the orexigenic peptide ghrelin increases whereas genetic or pharmacological suppression of the ghrelin receptor attenuates alcohol-mediated behaviors in rodents. In subsequent studies we verified this link between appetite regulatory peptides and addiction by showing that glucagon-like peptide 1 (GLP-1) analogues attenuate the ability of alcohol, as well as other addictive drugs, to increase accumbal dopamine release, cause a locomotor stimulation as well as induced a conditioned place preference in mice. In addition, activation of GLP-1 receptors reduces alcohol intake in various models of alcohol dependence. Another anorexigenic peptide displaying an ability to modulate reinforcement is amylin. Thus, we showed that acute administration of an amylin receptor agonist, sCT, attenuated the established effects of alcohol on the mesolimbic dopamine system, prevents relapse drinking and reduces the motivation to consume alcohol, but did not alter peanut butter intake. Furthermore, acute as well as repeated peripheral administration of sCT decreases alcohol intake in rats. In conclusion the present data support the hypothesis that appetite regulatory hormones regulate development of alcohol dependence and could be considered for the treatment of alcohol dependence in humans.

10:00 **The Ghrelin System In Alcohol Use Disorder: A Translational Approach**

L LEGGIO[1,2]

[1]CPN Section, NIAAA and NIDA, NIH, Bethesda, MD, United States, [2]Brown University, Providence, RI, United States

Dr. Leggio will present recent human data on the stomach-derived hormone ghrelin in AUD. Preliminary clinical studies indicate that there is a relationship between endogenous blood ghrelin levels and drinking status and craving for alcohol in patients with AUD. A double-blind placebo-controlled human laboratory study demonstrated, for the first time, that intravenous administration of exogenous ghrelin resulted in acute increase of cue-induced alcohol craving in a bar-lab setting. More recently, another double-blind placebo-controlled human laboratory study indicated that intravenous administration of exogenous ghrelin results in increased alcohol self-administration and differentially modulates brain activity during alcohol versus food cues while patients are performing a fMRI-based reward task (data in press). Additionally, unpublished data will be presented on how pharmacological manipulations of ghrelin signaling may result in changes in other gut-brain neuroendocrine pathways and the significance of these results will be discussed. Altogether, these findings suggest that blocking the ghrelin receptor may be a novel pharmacological approach to treat AUD. Specific to this discussion, two sets of unpublished data will be presented: 1) recent ongoing efforts toward the development of a novel ghrelin receptor knock-out rat model; and 2) recent human preliminary data testing a novel ghrelin receptor inverse agonist in individuals with AUD. Together, this line of research supports additional efforts aimed to investigate whether the ghrelin system may represent a novel potential target for medication development for AUD.

8:30 - 10:30 AM	Calusa FGH
ORAL SESSION 6: Fluid Balance	

Chair(s): Derek Daniels and Jessica Santollo

8:30 **Stage Of The Estrous Cycle Influences Cognitive Deficits After Extracellular Dehydration.**

J. SANTOLLO, K. MYERS, I.L. RAINER, M. MONTGOMERY
Dept. of Biology, University of Kentucky, Lexington, KY, United States

Dehydration induced by 24 h water deprivation impairs cognitive performance in male rodents. Estrogens have both protective effects on fluid regulation and improve performance in cognitive tasks. We, therefore, tested whether sex and stage of the estrous cycle would influence cognitive deficits that result from dehydration. Because 24h water deprivation induces both extracellular and intracellular dehydration, we tested which form of dehydration accounts for the deficits previously reported. Male and female rats were tested in a 5 day novel-object recognition task that included a habituation session, 3 5min training trails with identical objects, and a 5min test trail with the original and a novel object. Females were tested in either diestrus or estrus to account for differences in endogenous estradiol levels. On test day, rats (n=48) were treated with 2M NaCl or control to examine the effects of intracellular dehydration or rats (n=48) were treated with 20 μg/kg furosemide or control to examine the effects of extracellular dehydration. For the intracellular dehydration manipulation, all groups of rats, regardless of hormone or hydration status, spent significantly more time investigating the novel object ($p< 0.05$). For the extracellular dehydration manipulation, both the dehydrated and euhydrated males and estrous females spend significantly more time investigating the novel object ($p< 0.05$). The euhydrated diestrous females spend significantly more time investigating the novel object ($p< 0.05$), however, the dehydrated diestrous females spent a similar amount of time investigating the novel and familiar object (p=n.s.). Together this suggests that extracellular dehydration can induce deficits in recognition memory which can be rescued by hormone status in females.

8:45 **Regulation Of Water Intake By Eicosanoid Signalling In The Subfornical Organ**

DP BEGG
UNSW Sydney, Sydney, Australia

Water intake is reduced in response to dipsogenic stimuli in aging. We have previously reported that dietary ω-3 fatty acid inhibition of the arachidonic acid (AA)-cyclooxygenase (COX)-eicosanoid pathway can prevent the dysfunction in mechanisms controlling water intake in aging animals. With these experiments we aimed to determine the role of the AA-COX-eicosanoid pathway in water intake. To achieve this aim we targeted the expression of the gene for cytosolic phospholipase A2 ($cPLA_2$), which is involved in the synthesis of eicosanoids due to freeing the ω-6 fatty acid AA from cell membranes. It has previously been established that $cPLA_2$ is elevated in aging. $cPLA_2$ was targeted using AAV overexpression directly in the SFO, to examine if an “aging” thirst phenotype could be induced in young adult mice. Twelve week old mice were infected with AAV2-$cPLA_2$ with a GFP reporter into the SFO. Four weeks after viral transfections mice were dehydrated for 24 hours to induce a mixed hypovolemic/hyperosmotic state. Similar to observations in aged mice, young adult animals with an upregulation of $cPLA_2$ in the SFO displayed a suppression of fluid intake in response to dehydration, and reduced operant responding for water following hypertonic saline injection. Importantly, basal fluid intake was not affected in either aged or $cPLA_2$ overexpressing mice, demonstrating the potential for specificity in this model of the aging thirst response. Finally, $cPLA_2$ activity was elevated, similar to the affect observed in aged mice, ultimately leading to elevated PGE_2 levels. These data provide a potential model for the reduced fluid intake that occurs in aging and a target for restoration of fluid intake.

9:00 **Parsing &Lsquo;Angiotensin Sensitive&Rsquo; Neuronal Circuits Arising From The Lamina Terminalis: Implications For Endocrine, Autonomic And Behavioral Responses Mediating Body Fluid Homeostasis.**

AR ALLEYNE, K CAHILL, MD SMELTZER, EB BRUCE, Y TAN, SW HARDEN, CJ FRAIZER, AD DE KLOET, EG KRAUSE
University of Florida, Gainesville, FL, United States

Angiotensin type-1a (AT1a) receptors (AT1a) in the brain coordinate humoral, autonomic and behavioral responses that maintain body fluid homeostasis; but the neural circuits that mediate these effects are unclear. This study investigates the structure and function of AT1a neurons in the median preoptic nucleus (MnPO) and organum vasculosum of the lamina terminalis (OVLT), to evaluate their role in body fluid homeostasis. Using male AT1a-Cre mice, studies combined genetic reporting with *in situ* hybridization to reveal that AT1a neurons in the MnPO and OVLT are largely glutamatergic. Subsequently, AT1a-Cre mice were delivered a Cre-inducible adeno-associated virus to induce expression of channelrhodopsin-2 (ChR2) and yellow fluorescent protein (eYFP) within AT1a neurons of the MnPO/OVLT. Neuroanatomical and electrophysiological studies revealed that AT1a neurons in the MnPO/OVLT send glutamatergic projections to the paraventricular nucleus of the hypothalamus that synapse onto vasopressin (AVP) neurons. To evaluate functionality, we optogenetically stimulated these AT1a-expressing neurons while recording cardiovascular

parameters. Relative to control mice, 10 min of optogenetic stimulation robustly elevated blood pressure in mice expressing ChR2. This effect was rapid in onset and persisted for the 50 min of cardiovascular recording. Intriguingly, optogenetic stimulation elicited an increase in Fos induction in AVP neurons within the PVN. Lastly, optogenetic stimulation of these neurons in conscious freely-moving mice significantly increased both water and 0.3M NaCl consumption, while their inhibition had the opposite effect. These results suggest that AT1a neurons in the MnPO/OVLT mediate endocrine, autonomic and behavioral responses that maintain body fluid homeostasis.

9:15 **Oxytocin Receptor Agonist Injection Into The Parabrachial Nucleus Decreases Fluid Intake.**

PJ RYAN[1,2], RD PALMITER[1]

[1]Howard Hughes Medical Institute, University of Washington, Seattle, WA, United States, [2]Florey Institute of Neuroscience and Mental Health, Melbourne, Australia

This project aims to determine the effect of injecting oxytocin receptor agonist (TGOT) into the parabrachial nucleus (PBN) on fluid intake. A recent study identified oxytocin receptor-expressing neurons in the PBN ($Oxtr^{PBN}$) as key regulators of fluid intake (Ryan PJ *et al*, 2017, *Nat Neurosci*). Chemogenetic activation of $Oxtr^{PBN}$ neurons in mice robustly suppressed fluid, but not food or salt intake following salt depletion. $Oxtr^{PBN}$ neurons also demonstrate increased calcium activity when drinking water, but not a liquid diet or empty bottle, suggesting a selective role in fluid satiation. $Oxtr^{PBN}$ neurons increase spiking *in vitro* following application of a selective oxytocin receptor agonist, TGOT (200 nM); however, the effect of injecting TGOT into the PBN on fluid intake remains unknown. To investigate this, we implanted cannula over the PBN (n = 14 mice). Mice were subjected to a 2-bottle choice paradigm of water and 0.3 M saline (NaCl). Following habituation, we removed all fluid for 24 h. We then infused TGOT (200 nM; 500 nL) or saline over 2 minutes then returned fluid; which was repeated in a cross-design manner. There was a significant decrease in total fluid intake (2-way RM ANOVA; interaction $F(8,112) = 2.408$; $P = 0.0195$); however, the effect on fluid intake was not as robust as chemogenetic stimulation of $Oxtr^{PBN}$ neurons (20% vs 71% decrease). These results suggest that oxytocin provides only part of the effect on fluid inhibition.

9:30 **Development And Validation Of A New &Ldquo;Drinkometer&Rdquo; Device For The Direct Measurement Of Drinking Microstructure In Humans.**

D GERO[1], B FILE[2,3], J JUSTIZ[4], RE STEINERT[1], L FRICK[1], AC SPECTOR[5], M BUETER[1]

[1]Department of Visceral Surgery and Transplantation, University Hospital Zurich, Zürich, Switzerland, [2]Faculty of Information Technology and Bionics, Pázmány Péter Catholic University, Budapest, Hungary, [3]Wigner Research Centre for Physics, Hungarian Academy of Sciences, Budapest, Hungary, [4]Human-Centered Engineering Institute of Applied Sciences, Biel, Switzerland, [5]Department of Psychology and Program in Neuroscience, Florida State University, Tallahassee, FL, United States

Microstructural analysis of ingestive behavior offers the possibility to assess the role of metabolic state, oresensory signals, nutritional content and postingestive events in the temporal organization of ingestion. Our aim was to develop a device ("*drinkometer*") that captures ingestive microstructure (sucks and bursts) of an entire drinking episode in high definition (sampling: 1kHz). As a proof of concept study, we presented 8 concentrations of sucrose (0 – 280mM) in a blinded and random fashion, to 12 healthy adults under fasted or non-fasted states. We found that total kcal intake during drinking sessions was dependent on sucrose concentration ($P < .001$) and fasting state ($P = .009$), while total drinking time ($P < .001$), total volume consumed ($P = .003$), number of sucks in total ($P < .001$) and number of sucks per burst ($P = .04$), mean burst duration ($P = .03$) and mean burst speed ($P = .02$) was dependent on the fasting state. In contrast, volume per suck ($P = .002$), average suck speed ($P < .001$), and maximal speed per suck ($P < .001$) depended on sucrose concentration. Average speed of drinking ($P = .006$) and volume per burst ($P < .001$) were not influenced by sucrose concentration or by fasting state, but decreased significantly with meal progress when the first half of the bursts was compared with the second half within the same session. Notable and significant sex differences in drinking microstructure were observed. We conclude that the drinkometer is able to detect differences in patterns of human drinking behavior as a function of key experimental variables such as taste, caloric content, and physiological state. Accordingly, the drinkometer has the potential to reveal fundmental principles underlying the temporal organization of human ingestive behavior.

9:45 **Assessing A Strategy That Increased Liking For A Low Sodium Food In Adults Among Children**

N BOBOWSKI[1,2], JA MENNELLA[1]

[1]Monell Chemical Senses Center, Philadelphia, PA, United States, [2]St. Catherine University, St. Paul, MN, United States

Like sweet taste, children most prefer higher levels of salt than do adults. Not only are taste preferences elevated but their dietary intakes of sodium

and added sugars greatly exceed recommended levels. Experimental studies have shown that adults like the taste of a low-sodium food more after 3 weeks of repeated ingestion (3 occasions per week). Because this strategy has never been studied in pediatric populations, we determined whether repeated exposure to a low-sodium breakfast cereal increases children's liking of that food and alters salty and sweet taste preferences. Children who were regular consumers of breakfast cereals were randomized to one of two treatment groups: they ingested either a low-sodium (80mg sodium/cup) (N=20) or a regular (204mg sodium/cup) (N=19) cereal on at least 4 occasions per week for an 8-week trial. Children were phenotyped at baseline, midway (4 weeks) and at 8 weeks to determine level of saltiness and sweetness most preferred and which of the two cereals tasted better. Dietary recalls and measures of compliance were also assessed. We found no significant effect of treatment in children's liking of low-sodium cereal, most preferred level of salt or sucrose, daily sodium or added sugar intake, or adherence to protocol. However, throughout the trial, the child's most preferred level of salt was significantly correlated with most preferred level of sweet (all p's≤0.04), a finding consistent with prior research illustrating these taste preferences are heightened during periods of growth. Further research is needed to determine whether focusing on overall diet rather than a single food, and on both sweet and salt rather than salt alone, is effective in reducing the biologically-driven proclivity for salty and sweet tastes during childhood.

10:00 **Lateral Hypothalamic Neurotensin Neurons Orchestrate Drinking Behavior**

G KURT, S FOWLER, HL WOODWORTH, R BUGESCU, GM LEINNINGER
Michigan State University, East Lansing, MI, United States

The brain detects fluid and energy status and coordinates the appropriate ingestive behavior (drinking or feeding) to resolve imbalance. Yet, there remains incomplete understanding of the neurons bridging sensory detection and behavioral output, and thus how the brain selects for drinking vs. feeding. We examined the role of neurotensin-expressing neurons of the lateral hypothalamic area (e.g. LHA^{Nts} neurons) in coordinating ingestive behaviors. Using a viral monosynaptic tract tracing strategy, we found that LHA^{Nts} neurons receive direct inputs from both osmolality and energy sensing brain regions. Anterograde tract tracing revealed that LHA^{Nts} neurons densely project to two sites in the brain: the ventral tegmental area (VTA) and the lateral preoptic area (LPO) implicated in modulating feeding and drinking, respectively. While activation of other LHA populations induces generalized feeding and drinking, DREADD-mediated activation of LHA^{Nts} neurons specifically induced voracious drinking behavior, but not feeding. Intriguingly, LHA^{Nts} neuronal activation prompted mice to consume any available solution, but they preferred water or palatable saline solution over a bitter quinine solution, suggesting that their taste remained intact. Overall, our data suggest that LHA^{Nts} neurons bridge sensory and behavioral centers, and that their activation favors drinking behavior over feeding. Thus, LHA^{Nts} neurons may be important coordinators of drinking behavior needed to maintain fluid homeostasis.

10:15 **Thirst And The Hormone Angiotensin Ii Recruit Vta Dopamine Signalling To Water Availability**

TM HSU, VR KONANUR, MF ROITMAN
Dept. of Psychology, University of Illinois at Chicago, Chicago, IL, United States

Changes in physiological state, including hunger, satiety, and body fluid perturbations, can strongly modulate mesolimbic dopamine signalling and reward encoding. Here we examine the novel hypothesis that thirst potentiates the encoding of water cues by VTA phasic dopamine activity. To capture dopamine neural activity in awake animals, we utilized in vivo fiber photometry in rats expressing Cre-recombinase under the control of a tyrosine hydroxylase promoter (TH-Cre+) together with a Cre-dependent AAV packaged with a Ca^{2+} indicator, GCaMP6f targeting the VTA (AAV1-Syn-Flex-GCaMP6f). In water-restricted animals allowed intermittent sipper access, our results first demonstrated that VTA dopamine neurons acquire robust Ca^{2+} activity in response to cues associated with water. Interestingly, after training under water-restriction, we find a lack of cue-evoked VTA Ca^{2+} activity in water-sated animals. To investigate whether central hormone modulation can mimic thirst in recruiting VTA dopamine responses, we delivered the dispogenic hormone, Angiotensin II (AngII) to the lateral ventricles of water-sated TH-Cre+ rats. We found that in water-sated rats treated with AngII, but not vehicle, the water cue evoked a Ca^{2+} response remarkably similar to that observed in water-restricted rats. Finally, in both water-restricted and AngII-treated rats we found a negative correlation between the magnitude of the cue/licking-evoked VTA Ca^{2+} signal and number

of trials; data that suggests that VTA dopamine neurons can relay subtle changes in physiological state as water is consumed. Overall, our findings reveal that thirst can powerfully influence VTA dopamine activity and highlights the importance of physiological state in mediating mesolimbic dopamine function.

10:30 - 11:00 AM	Calusa DE
Coffee Break	

11:00 - 12:00 PM	Calusa ABC
MARS LECTURE 3	

Chair(s): Carrie Ferrario

11:00 **Individual Variation In Resisting Temptation: Implications For Impulse Control Disorders**
TE ROBINSON
University of Michigan, Ann Arbor, MI, United States

Cues (conditioned stimuli, CSs) that are associated with rewards can act as powerful temptations, leading to maladaptive behavior, such as overeating, or, in the case of drug cues, relapse. However, such cues come to exert powerful control over motivated behavior only if they are attributed with incentive salience, and thus aquire the ability to act as incentive stimuli. There is, however, considerable individual variation in the extent to which CSs acquire incentive motivational properties. This is important because only if CSs act as incentive stimuli do they come to attract, provoke and motivate, leading to potentially maladaptive behavior. This talk will first review studies showing that some rats (called sign-trackers, STs) are especially prone to attribute incentive salience to discrete food cues, relative to others (called goal-trackers, GTs). Variation in the propensity to attribute incentive salience to reward cues appears to be due to variation in dopamine neurotransmission. Interestingly, STs and GTs also differ in the degree of executive (inhibitory) control they can exert over behavior when faced with temptations, and this is related to variation in prefrontal cholinergic neurotransmission. It will be suggested that it is this interaction between a hyperactive “bottom-up” dopamine-mediated motivational system and a hypoactive “top-down” acetylcholine-mediated executive control system that results in some animals (STs) having particular difficulty resisting temptation, making them more susceptible to impulse control disorders, including overeating.

12:15 - 4:15 PM	Calusa Foyer
Lunch on Own	

Salads, Sandwiches, Hamburgers and Hot Dogs will be available for purchase by CASH or hotel room charge in the Calusa Foyer. Price Range ($10-$15)

12:15 - 1:45 PM	Great Egret
Professional Development: Job Fair and Forum	

The job fair is designed to expand the horizons of young scientists in pursuit of their careers in science as well as increasing their network. The participants should gain an insight into careers in industry, academia, government, and others. There will be short talks by the experts from different areas, followed by round table talks where the participants can have the chance to speak with the experts. We will also have a board with job postings and a sign-up sheet for people who are hiring to meet talented young scientists.

Chair(s): Shin Jae Lee and Dawna Venzon

2:00 - 3:00 PM	Calusa ABC
Publishing Connect Workshop	

After attending this free workshop, one in the Elsevier Publishing Connect Workshop series, early career researchers will be given an idea of the steps required to be taken before starting to write a paper. They will also be able to plan writing manuscripts using the logical step sequence, not the sequence in which the paper will be read. Authors are also made aware of what aspects of their papers Editors, Reviewers, and Publishers look at critically, and can ensure that in taking care of these areas, their papers are more likely to be accepted. Sensitive areas such as publishing ethics, plagiarism, duplicate publishing, etc. are also explained such that participants have an understanding of what their responsibilities are, what is allowed, and what is not permitted. At least two Editors of Elsevier journals will also be on hand to answer questions.

4:00 - 6:00 PM	Calusa ABC
Symposium 5: THE STRESS, DEPRESSION AND EATING ROUNDABOUT	

Chair(s): Dana Small and Susanne la Fleur

4:00 **Role Of Stress Neurobiology And Metabolic Hormone Interactions In Food Reward, Overeating And Obesity**
R SINHA
Yale Interdisciplinary Stress Center, Departments of Psychiatry, Neuroscience and Child Study, Yale University School of Medicine, New Haven, CT

Obesity is a global epidemic and behavioral, lifestyle and other pharmacological interventions are only modestly effective in reducing obesity. Stress and affect are key triggers for excessive consumption of highly palatable foods that promote overeating and weight gain. Findings from recent studies on how the brain loses control over regulation and control of highly palatable food intake will be shown, and the role of stress and motivation brain pathways in this process will be the focus of the talk. The presentation will focus on brain systems involved in central and peripheral stress and metabolic responses during food intake will be discussed. Overlap in brain circuits regulating food intake and those that drive stress regulation will be shown. Finally, role of the medial prefrontal brain systems in regulating stress, emotions, and food craving and self control over food intake will be discussed to illustrate that disruption of such control may promote excessive intake of highly palatable foods.

4:30 **Sweet Cognition: Glucose Facilitates Attention To Food Cues In Individuals With Obesity**
AE MASON
UCSF Osher Center for Integrative Medicine, San Francisco, CA, United States

Glucose improves cognitive performance. It is unknown whether glucose enhances attentional food bias (which we term “sweet cognition”), and how BMI status impacts this phenomenon. We posited that people of obese BMI status (versus lean status) would experience greater facilitation of attentional food bias after consuming a 75g glucose beverage (sweet cognition: ΔATT-Food), and that glucose-induced changes in attentional food bias would correlate with non-homeostatic eating of sugary foods, poorer glycemic control, and stress-relief. Participants (N=35) completed the n-back, a cognitive task modified to assess attentional food bias (ATT-Food) by contrasting accuracy on food versus non-food cues. They provided blood once fasted and once 60-min after drinking a 75g glucose beverage (Glutol). We computed pre-post changes in blood glucose and insulin (ΔBG & ΔBI), sweet cognition (ΔATT-Food), and perceived task-stress (Δstress). After the second cognitive test and blood draw, participants ate lunch and “taste tested” highly palatable foods (measured). Ingestion of 75g glucose provoked increases in ΔATT-Food in participants of obese (relative to lean) BMI status (F(1,33)=5.12, p=.031). Greater ΔATT-Food correlated with greater ΔBG (r=.46, p=.007) and reduced Δstress (r=-.42, p=.011), and nearly correlated with eating sweets during the taste test (r=.33, p=.057) but not with ΔBI. Thus, an index of sweet cognition may help identify people who may benefit from cognitive retraining or neuromodulation interventions.

5:00 **Prenatal Adversity And Behavioral Reactivity To Food Stimuli: Insulin Modulation Of The Brain Dopamine Pathways**
PP SILVEIRA
Department of Psychiatry, McGill University, Montreal, QC, Canada

Poor growth during early life, a marker of exposure to prenatal adversity, persistently shifts the energy balance towards storage of body fat, and is associated with increased risk for developing diseases such as type II diabetes in adulthood. We have described the relationship between poor fetal growth and the development of hedonic eating, exploring the neurobiological mechanisms that drive these behaviors. Our group has demonstrated both in animal models and humans that variations in the mesocorticolimbic dopaminergic function are involved in the differential behavioral responses to palatable foods in individuals exposed to poor fetal growth. Small and persistent changes in food preferences and feeding behaviors progressively deteriorate the metabolic profile of these individuals, and contribute to the establishment of their health/disease patterns, leading to increased risk for several chronic conditions including cardiovascular disease, type II diabetes and mental health issues. Dopamine is a key neurotransmitter modulating the behavioral response to natural and drug rewards, mainly through projections from the ventral tegmental area (VTA) into the nucleus accumbens (NAcc). The exposure to non-optimal fetal growth seems to persistently modify the relationship between a) insulin, that

signals energy and glucose homeostasis and modulates DA release through its action on the VTA, b) dopamine function and c) behavioral response to reward. We are interested in understanding the interface between prenatal adversity, metabolism, neurochemistry and behavior, aiming to identify factors associated with vulnerability to adult metabolic conditions and their co-morbidities, and better inform the development of preventive measures and treatment.

5:30 **Dietary And Neural Components Of Obesity-Induced Mood Deficits**

S FULTON[1,2,3,4]

[1]University of Montreal, Montreal, QC, Canada, [2]Center for Studies in Behavioral Neurobiology (Concordia University), Montreal, QC, Canada, [3]Montreal Diabetes Research Center, Montreal, QC, Canada, [4]CHUM Research Center, Montreal, QC, Canada

The incidence of anxiety and depressive disorders is significantly compounded by obesity. Obesity arising from excessive intake of high-fat/high-sugar food provokes anxiodepressive behavior in mice and elicits molecular adaptations in the nucleus accumbens, a region well-implicated in the hedonic deficits associated with depression and motivated behavior. We found diet-induced obesity leads to anxiodepressive behaviour, in a manner relying on the type of dietary fat consumed (saturated), ensuing metabolic inflammation and neuroimmune activity in the nucleus accumbens. In contrast, increased intake of omega-3 polyunsaturated fatty acids can have antidepressant actions. The impact of food and metabolic dysfunction on mood will be discussed: Findings will be presented describing some of the metabolic, immune and neural mechanisms underlying the impact of caloric overload on anxiodepressive behaviour. In addition, recent data will be presented on the neuroprotective actions of GPR120, a g-protein coupled receptor activated by omega-3 fatty acids that is predominantly expressed in microglia. Via microglia-specific GPR120 gene ablation and GPR120 pharmacological activation we show that GPR120 has a fundamental role to play in metabolic inflammation and mood regulation.

4:00 - 6:00 PM	Calusa FGH
Oral Session 7: Development	

Chair(s): Susan Carnell and Miranda Johnson

4:00 **Effects Of Hunger State On The Neural Correlates Of Food Choice Across The Lifespan**

L CHARBONNIER[1], F VAN MEER[1], D CRABTREE[2], W BUOSI[2], A GIANNOPOULOU[3], O ANDROUTSOS[3], AM JOHNSTONE[2], Y MANIOS[3], PAM SMEETS[1]

[1]University Medical Center Utrecht, Utrecht, Netherlands, [2]University of Aberdeen, Aberdeen, United Kingdom, [3]Harokopio University Athens, Athens, Greece

Food choices determine energy intake and thus play a crucial role in weight management and health across the lifespan. It is unknown how development and aging influence food decision making and how hunger state may impact on this. We examined how food choices and associated brain activation are modulated by hunger state and age. Data from 95 participants were analyzed (18 children, 25 teens, 27 adults, 25 elderly). They performed a food choice task during fMRI, either fasted or sated. In this task they made 100 choices between low- and high-calorie food pairs matched on liking. Elderly chose more low-cal foods than the other groups. Overall, more high-cal foods were chosen during hunger. However, hunger state did not affect food choice-related brain activation. During food choice children/teens had lower dorsolateral prefrontal cortex (dlPFC) and visual processing area activation compared to adults/elderly. Also, children/teens had lower reaction times during high-cal choices than adults/elderly. There were no interactions between hunger state and age group. Caloric content of chosen foods negatively modulated primary visual cortex activation during hunger, while the opposite was true after satiation. In conclusion, it may be harder for children/teens to resist high-cal foods because of their reduced inhibitory capacity, as corroborated by their overall lower dlPFC activation during food choice and their faster responses for high-cal foods (despite similar liking of the choice options). Hunger appears to lessen attention during high-cal food choices across all ages, which may promote overconsumption as suggested by the greater proportion of high-cal food choices during hunger. Probing these vulnerabilities with neuroimaging may provide targets for prevention of overconsumption.

4:15 **Sex Differences In The Impact Of Portion Size And Energy Density On Children&Rsquo;S Neural Responses To Food Images**

BA FUCHS[1], TP MASTERSON[1], EG BRIAN[1], LK ENGLISH[1], SN FEARNBACH[2], M LASSCHUIJT[3], SJ WILSON[4], BJ ROLLS[1], AL PEARCE[1], KL KELLER[1,5]

[1]The Pennsylvania State University, Department of Nutritional Sciences, University Park, PA, United States, [2]Pennington Biomedical Research Center, Baton Rouge, LA, United States, [3]Wageningen University & Research, Division of Human Nutrition, Wageningen, Netherlands, [4]The Pennsylvania State University, Department of Psychology, University Park, PA, United States, [5]The Pennsylvania State University, Department of Food Science, University Park, PA, United States

Large portions of high energy-dense foods increase energy intake in children, which may contribute to the development of obesity. We previously used a region-of-interest analysis to demonstrate sex-differences in children’s responses to food portion size (PS) and energy density (ED) in brain regions implicated in reward, valuation, and emotion. To extend these findings, we conducted a whole-brain analysis to test for sex differences in neural responses to food images varied by PS and ED. In a block-design fMRI paradigm, 48 children (N=23 boys, 7-10 yrs) viewed food images at two levels of ED (high, low) and PS (large, small). Repeated measures ANOVA tested for differences in blood-oxygen level dependent responses to food cues between boys and girls. Beta values were extracted from clusters demonstrating differential activation by sex, and post-hoc analyses were run after controlling for BMIz and food image liking/wanting. Results showed sex x PS interactions in the visual cortex, fusiform gyrus, putamen, hippocampus and cingulate (all $P < 0.001$). In all regions, girls, but not boys, showed greater responses to large vs. small PS. In the putamen, these effects were driven by increased activation among girls to the large PS, high-ED cues. Boys showed an opposite response pattern in the putamen, with greater activation to smaller portions, particularly to low-ED foods. These results extend our previous findings by demonstrating that girls and boys also process food cues differently in regions implicated in visual processing and memory. Future analyses are needed to explore the etiology and behavioral implications of these differences. This work may inform the development of more effective, personalized approaches to reduce overeating in the presence of large portion sizes.

4:30 **Children Who Have Higher Baseline Food Responsiveness Benefit More From A Technology-Based Behavioral Intervention To Improve Food Intake Regulation**

NA REIGH[1], SL O'NEILL[1], AL KRAMER[1], BJ ROLLS[1], JS SAVAGE[1], SL JOHNSON[2], B LOHSE[3], HT ZIMMERMAN[4], KL KELLER[1, 5]

[1]The Pennsylvania State University, Department of Nutritional Sciences, University Park, PA, United States, [2]The University of Colorado Medical Center, Department of Pediatrics, Aurora, CO, United States, [3]The Rochester Institute of Technology, Wegman's School of Health and Nutrition, Rochester, NY, United States, [4]The Pennsylvania State University, Department of Learning and Performance Systems, University Park, PA, United States, [5]The Pennsylvania State University, Department of Food Sciences, University Park, PA, United States

Food intake regulation is critical for maintaining energy balance. We conducted a study to evaluate the efficacy of a laboratory-based food intake regulation intervention that used a virtual reality game to teach children to respond to hunger and fullness signals. We hypothesized that child appetitive traits, satiety responsiveness (SR) and food responsiveness (FR), would be associated with improvements in food intake regulation such that children with high FR and low SR would show greater improvements across the intervention. A within-subjects study tested 28 children (mean age 5.0±0.8 y; 16 boys) to examine the effect of the technology-enhanced intervention on children's change in energy compensation (COMPx) across a 10-wk study that included the 4-wk intervention. Parents reported child FR and SR on the Children's Eating Behavior Questionnaire at baseline. Compensation ability was assessed pre- and post-intervention using high-kcal (150 kcal) and low-kcal (3 kcal) liquid preloads. Overall, COMPx improved with the intervention (P=0.01). Repeated measures mixed models showed a FR x time interaction on COMPx (P=0.04); children with higher baseline FR showed greater improvements in COMPx relative to children with lower baseline FR. Further, a trend for a SR x time interaction (P=0.06) suggested that children with lower baseline SR showed greater increases in COMPx over time. No significant effects of covariates (BMIz, age and sex) were found. These findings suggest that a virtual-reality food intake game, a cost-effective and sustainable delivery model, may improve food intake regulation, particularly in children who start with high FR and low SR. These characteristics may aid in the development of targeted approaches to improve food intake regulation in children.

4:45 **Maternal And Early-Life Diet Dictates Bodyweight Gain And Alters Hindbrain Plasticity In Offspring.**

CG LIBERINI, LM STEIN, M GHIDEWON, AN CORINI, T LING, L LHAMO, MR HAYES
Department of Psychiatry, University of Pennsylvania, Philadelphia, PA, United States

While previous studies highlight the detrimental impact of *in utero* and postnatal exposure to high-fat diet (HFD) on offspring propensity to develop obesity, the neurobiological mechanisms underlying this outcome are not well understood. Here, we show that maternal and postnatal consumption of HFD dramatically alters the DVC cytoarchitecture via increased astrogliosis, putatively contributing to a predisposition of offspring to have reduced sensitivity to satiation signals and increase bodyweight gain. Further, as recent therapeutic strategies for treating obesity in adults have focused on targeting the glucagon-like peptide-1 (GLP-1) system, here we also examine whether the GLP-1 receptor agonist liraglutide could be used in juvenile rats as an anti-obesity pharmaceutical to prevent not only adolescent, but also adult obesity caused by maternal and early-life HFD overnutrition**.** Male and female rats were maintained on chow or HFD, according to the maternal diet. Animals received daily subcutaneous injection of liraglutide (50µg/kg, from postnatal day [PND]30-PND40; 200µg/kg from PND40-PND60) or vehicle. Our results show that chronic administration of liraglutide in juvenile rats prevented bodyweight gain and retained a normo-glycemic profile in males but not females. These preclinical data suggest that maternal and early-life HFD increases astrogliosis in the DVC, caloric intake and bodyweight gain – a collective set of unwanted metabolic effects that appear to be treatable in male juveniles with GLP-1R agonist pharmaceutical intervention. Support: FNSNF-P22HP3_172289

5:00 **Memory Impairments Associated With Early Life Sugar Consumption In Rats Are Functionally Related To Alterations In The Gut Microbiome**

EE NOBLE, RB JONES, MI GORAN, SE KANOSKI
University of Southern California, Los Angeles, CA, United States

We previously reported that habitual sugar consumption in rats during the juvenile and adolescent period of development significantly impairs hippocampal-dependent memory function. Here we sought to determine whether these effects are based, in part, on alterations in the gut microbiome. Juvenile rats (PN27) were fed chow and water *ad libitum* and were given access to either a sugar solution (11% weight by volume; 35% glucose, 65% fructose) or an extra bottle of water (controls). Following *ad libitum* access to the sugar solution (or extra water) for the entire juvenile/adolescent period (PN27-60), rats were tested in a hippocampal-dependent contextual episodic memory task (Novel Object in Context [NOIC]). Results revealed that NOIC memory performance in rats fed the sugar solution was significantly impaired relative to controls. Subsequent cecal and fecal16S rRNA analyses showed that rats fed sugar solution had a microbiota clustering pattern that was distinct from controls. To examine whether these alterations are functionally related to the memory deficits, naïve rats (PN27) received a microbiome transfer procedure that first involved 3 gavage treatments (over 7 days) with either saline or an antibiotic cocktail. Next rats received thrice weekly gavage treatments (for 2 weeks) of the fecal/cecal contents from donor rats fed either the sugar solution (Abx-Sugar) or from control rats (Abx-Control), whereas a second control group received saline gavage treatments only (Sal-Sal). Results from the NOIC memory task revealed that the Abx-Sugar group was significantly impaired compared to both control groups, suggesting that alterations in the gut microbiota may provide a mechanistic link between early life sugar consumption and hippocampal dysfunction.

5:15 **(Nita Award Winner) Developmental And Adult Overnutrition Alter Synaptic Inputs And Leptin Signaling Onto Proopiomelanocortin Neurons In The Arcuate Nucleus Of The Hypothalamus**

BL ROBERTS, CM BENNETT, SR LINDSLEY, P KIEVIT
Oregon National Primate Research Center, BEAVERTON, OR, United States

The arcuate nucleus of the hypothalamus (ARH) is a critical brain region involved in the homeostatic control of food intake and energy metabolism. Proopiomelanocortin (POMC) neurons in the ARH send projections throughout the brain and have a prominent role in regulating energy balance, promoting the suppression of food intake, and influencing glucose homeostasis. Maternal obesity, diet-induced obesity (DIO), diabetes, and leptin deficiency all alter the development of ARH projections. Here we characterize the synaptic development of ARH-POMC neurons and explore whether overnutrition during development or DIO alter synaptic inputs and leptin signaling onto ARH-POMC neurons. Using transgenic POMC-GFP mice, we generated a chronic postnatal overnutrition (CPO) model by culling litters of 7-9 pups to three (3) pups on postnatal (P) day 3, allowing higher access to the lactating mother which resulted in increased body weight. For our DIO model, POMC-GFP mice were placed on a high-fat diet (HFD) for 12-16 weeks. Whole-cell patch clamp techniques were used to record from ARH-POMC-GFP neurons in each mouse model. Here we show that leptin's effect on action potential firing in ARH-POMC-GFP neurons may undergo a 'leptin switch' coinciding with the leptin surge, as leptin primarily decreases action potential firing rate at age P7-9, has mixed effects at P13-15 and increases firing rate in adult ARH-POMC-GFP neurons. We also show that the leptin's effect on inhibitory inputs onto ARH-POMC-GFP neurons is decreased in both CPO and DIO mice. This data suggests that overnutrition during development and DIO alter synaptic inputs onto ARH-POMC neurons and their responses to leptin, both of which are key regulators of food intake and energy metabolism.

5:30 **Increasing Energy Density Of Unappetizing Foods Is Associated With Lower Weight Gain In Adolescents**

JR SADLER[1], GE SHEARRER[1], E STICE[2], KS BURGER[1]
[1]University of North Carolina- Chapel Hill, Chapel Hill, NC, United States, [2]Oregon Research Institute, Eugene, OR, United States

Highly energy dense foods are often synonymous with high palatability. However, food preferences can depend heavily on individual differences. Food preferences are closely related to food intake, which can impact weight change over time. We examined whether the energy density (ED) of self-selected appetizing and unappetizing food images related to baseline BMI and 4-year change in adolescents (n=117; 45%M, baseline BMI:21.11.9. Participants completed hedonic VAS (-350 to 350) ratings of 103 food images, of which pleasantness was used to form groups. The 32 highest rated images were classified as appetizing, and the 32 lowest rated images, excluding those rated as disgusting (-350), were classified as unappetizing. Average energy density of images in the appetizing and unappetizing sets were calculated for each participant. Regression analyses were used to test the relationship between energy density and baseline BMI and 4-year BMI slope, with significance considered at $p< 0.05$. No significant relationship was observed when appetizing food ED or unappetizing food ED was regressed on baseline BMI (p's=0.20,0.22). There was a significant interaction between energy density and hedonic value driven by an inverse relation between unappetizing food energy density and BMI change (p=0.008). Specifically, participants who rated higher energy dense foods as unappetizing showed less weight gain (=-0.13, p=0.014). There was no significant relationship between energy density of appetizing foods and weight change (p=0.67), suggesting that dislike of highly energy dense foods more strongly associates with lower weight gain than preference for low energy dense foods. Results support that lack of preference for highly caloric foods is a determinant of weight change in adolescents.

5:45 **Neural Correlates Of Appetitive Characteristics In Adolescents**

S CARNELL, A PAPANTONI, L CHEN
Johns Hopkins University School of Medicine, Baltimore, MD, United States

Our goal was to investigate the neural correlates of commonly assessed, weight-associated appetitive characteristics in youth. Seventy-nine adolescents (14-18 y; mean BMIz 0.61±1.20; 40F, 39M) varying in familial obesity risk viewed pictures of high energy density (ED) foods, low-ED foods and non-foods, following consumption of a 474 ml preload composed of water (0 kcal, fasted condition) or milkshake (480 kcal, fed condition). Following scanning, a multi-item ad-libitum buffet was administered. Food approach was assessed by the parent-report Child Eating Behavior Questionnaire (CEBQ) (Food Responsiveness, FR; Enjoyment of Food, EF; Emotional Overeating, EOE). Food avoidance was assessed by CEBQ-Satiety Responsiveness (SR), and by caloric compensation scores reflecting the percentage of the preload calorie difference that was effectively compensated for by relative down-regulation of meal intake in the fed condition. Preliminary whole-brain analyses ($p< 0.001$ uncorrected) comparing responses to high-ED vs low-ED food cues revealed that higher FR, EF & EOE were associated with greater insula and putamen activation in the fasted state. Higher EOE was additionally associated with greater hippocampus and amygdala activation in the fed state. Higher COMPX was associated with lesser insula response in the fed state. Higher FR and EOE were associated with greater child BMIz (r=0.25, p=0.026) (r=0.383, $p< 0.001$) and higher SR with lower child BMIz (r=-0.30, p=0.007). Our results illuminate neural circuits underlying appetitive characteristics commonly measured by questionnaires or behavioral tests. Future analyses will take a neural endophenotype approach to understand shared and independent neural circuits underlying these correlated but distinct eating styles.

6:00 - 8:00 PM	Calusa DE
POSTER SESSION III	

P71 **A Novel, Double Intra-Carotid Cannulation Technique To Study The Effect Of Central Nutrient Sensing On Glucose Metabolism In The Rat.**

L EGGELS[1], LL KOEKKOEK[1], M RIJNSBURGER[1], UA UNMEHOPA[1], MT ACKERMANS[3], S LUQUET[2], MJM SERLIE[1], SE LA FLEUR[1]

[1]Dept. of Endocrinology and Metabolism, AMC-UvA, Amsterdam, Netherlands, [2]Unit of Functional and Adaptive Biology, Paris Diderot Univ-Paris 7, Paris, France, [3]Dept. of Clinical Chemistry, Laboratory of Endocrinology, AMC-UvA, Amsterdam, Netherlands

The hypothalamus senses nutrients, responds to hormones and controls glucose balance. To study effects of nutrients and hormones on the brain intracerebroventricular injections or infusions via osmotic minipumps are frequently used techniques. However, these techniques bypass the blood-brain-barrier and represent a less physiological approach. Therefore, a more optimal solution would be to infuse via the circulation but directly towards the brain, which could be facilitated via the carotid artery. However, using the carotid artery limits the option to sample blood from the same artery, in experiments where the jugular vein is cannulated for infusion. We developed a double cannulation technique for the carotid artery, enabling us to infuse directly towards the brain, and to draw blood samples from the same artery, providing a physiological route to measure the effects of centrally infused substances. Together with an implanted jugular vein catheter, it is also feasible to continuously infuse stable isotopes to measure glucose (or lipid) kinetics, and draw blood samples in an undisturbed rat. Using this technique, we show that an infusion of Intralipid 20% and glucose (1%;IL+G), directly towards the brain, increases endogenous glucose production (EGP) significantly compared to infusion of IL or saline towards the brain (P=0.02; n=6-9). These infusions had no effect on plasma concentrations of corticosterone or insulin. To control for peripheral effects of IL+G, we also performed carotid infusions towards the general circulation (IL-GGC) and show no differences in EGP between IL+GGC and salineGC infused rats. Taken together, we present a novel double catheter technique, and show first data on effects of fat and sugar infusions towards the brain on EGP in an undisturbed rat.

P72 **Comparison Of Dreadd Agonists For Activation Of Orexin Neurons And Physical Activity.**

PE BUNNEY[1,2], MB JONES[3], CM KOTZ[2,3]

[1]Minnesota Obesity Prevention Training Program, University of Minnesota (UMN), Minneapolis, MN, United States, [2]Geriatric Research Education and Clinical Center, VA Health Care System, Minneapolis, MN, United States, [3]Department of Integrative Biology and Physiology, UMN , Minneapolis, MN, United States

Designer Receptors Exclusively Activated by Designer Drugs are used to selectively activate neurons in the brain via peripheral administration of clozapine N-oxide (CNO), a drug designed to bind exclusively to DREADDs. Recent evidence suggests that after injection, CNO is metabolized into clozapine, which can then bind to clozapine and/or DREADD receptors. Clozapine has sedative properties, which could confound results. We hypothesized that low clozapine doses would activate DREADDs to increase spontaneous physical activity (SPA), while high doses would reduce SPA. To test this, we compared CNO vs. clozapine on SPA in mice prepared with DREADDs on orexin neurons. Male and female orexin-cre+ mice (n=8) were individually housed in indirect calorimetry chambers and ascending doses of CNO (1-5mg/kg) and clozapine (0.001 – 5mg/kg) were administered every 48 h. SPA was significantly increased following 5mg/kg CNO ($F(5,35) = 213.4$; $p < 0.01$), beginning in the first h post-injection. The lowest doses of clozapine had no effect on SPA, but the intermediate doses (0.01 - 0.05mg/kg) reduced SPA beginning in h 10 ($F(5,35) = 169.6$; $p < 0.00$). The highest doses of clozapine increased SPA within the first 6 h, but then reduced SPA after 10 h ($F(3,35) = 93.78$; $p < 0.01$). One explanation for this could be that high doses of clozapine may interact with DREADDs in a similar time course as CNO to produce increases in SPA, which is then overcome by the sedative effects of the drug itself 10 h later. The highest doses of clozapine also increased food intake and reduced energy expenditure. Together these results indicate that the doses of clozapine that activate DREADDS have ancillary behavioral effects, precluding its use as a DREADD agonist in behavioral studies.

P73 **Pharmacological And Safety Analyses Of Subchronic Oral Metabocin^{Tm} Feeding In Mice**

P BASKARAN[1], L MARKERT[1], J BENNIS[1], L ZIMMERMAN[1], J FOX[2], B THYAGARAJAN[1]

[1]University of Wyoming School of Pharmacy, Laramie, WY, United States, [2]University of Wyoming, Dept. of Veterinary Sciences, Laramie, WY, United States

Obesity leads to metabolic complications. Recent research suggests that activation of transient receptor potential vanilloid subfamily 1 (TRPV1) by Metabocin^{TM} (also known as capsaicin) is a good strategy to counter diet-induced obesity. Previously, we have demonstrated that Metabocin^{TM}

countered obesity in mice without decreasing energy intake. However, there is lack of information on the safety of long-term oral feeding of Metabocin™. Here, we performed a dose relationship correlation between various doses of Metabocin™ and high fat diet (HFD)-induced obesity in wild type (WT) mice. We conducted a subchronic oral safety study for Metabocin™ in normal chow diet (NCD)-fed WT mice. We monitored body weight and energy intake in WT mice fed NCD (± Metabocin™) or HFD [(60% fat) ± Metabocin™] for eight months. We measured adipogenic and thermogenic gene/protein expression in the inguinal white adipose tissue (iWAT) from these mice, conducted histological studies of vital organs, measured inflammatory cytokines in plasma, and liver and kidney function tests. Metabocin™, above 0.001% in HFD, countered obesity and increased the expression of sirtuin-1 and uncoupling protein 1 in iWAT. HFD elevated alanine amino transferase and creatinine in blood, caused iWAT hypertrophy and hepatic steatosis, and Metabocin™ reversed these. Metabocin™ did not decrease body weight, food/water intake or cause any inflammation in NCD-fed mice. Our data suggest that Metabocin™ did not cause any systemic toxicities in WT mice but suppressed HFD-induced weight gain. Chronic oral feeding of Metabocin™ is safe and well tolerated by mice. Further studies in humans to evaluate the safety and efficacy of Metabocin™ is required to its use as a novel anti-obesity agent.

P74 **Use Of Real-Time Glucose Monitoring In Rats To Investigate Changes In Glucose Excursions And Hypoglycemia After Bariatric Surgery**

TA LUTZ, S SENN, CN BOYLE
Institute of Veterinary Physiology, University of Zurich, Zurich, Switzerland

Bariatric surgery, and specifically Roux-en-Y gastric bypass (RYGB), currently the most successful treatment of obesity, can also eliminate the need to treat type-2 diabetes. Unfortunately, RYGB patients also exhibit increased glycemic variability, spending more time in hyper- and hypoglycemic states, and are at increased risk of postprandial hypoglycemia, which can be fatal in the most severe cases. As the incidence of postprandial hypoglycemia increases, so does the importance of understanding this disabling complication and finding ways to control it. Our previous work showed that Zucker diabetic fatty (ZDF) rats undergoing RYGB were also prone to severe hypoglycemia, and even non-diabetic rats exhibit increased glycemic variability after RYGB. We therefore performed real-time glucose monitoring in ZDF rats following RYGB surgery. Food intake was also continuously monitored, allowing us to investigate the relationship between spontaneous meals and hypoglycemia. Because the pancreatic hormone amylin controls the rate of glucose appearance following a meal, we tested whether amylin or its agonist, salmon calcitonin (sCT), could minimize the initial postprandial glucose peak in an effort to reduce the ensuing hypoglycemia. Pre-prandial treatment with amylin or sCT appears to stabilize postprandial glucose, reducing glycemic variability. However, higher doses also promote hyperglycemia. Thus, amylin and its analogues represent potential candidates to treat postprandial hypoglycemia after RYGB, however additional studies are needed to understand appropriate dosing strategies and the precise mechanism through which amylin exerts these actions.

P75 **Novel Tools For Real Time *In Vivo* Glutamate Detection; Future Application In Ingestive Behavior**

D MISHRA[1,2,3], Y WANG[2], J BERGMAN[2], J KIEGHRON[2], KP SKIBICKA[1,3], AS CANS[2]
[1]Institute for Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden, [2]Department of Chemistry and Chemical Engineering, Chalmers University of Technology, Gothenburg, Sweden, [3]3Wallenberg Centre for molecular and translational medicine, University of Gothenburg, Gothenburg, Sweden

Glutamate is the most prevalent excitatory neurotransmitter in the mammalian central nervous system (CNS). It is necessary for all life functions, and dysfunction of the glutamate system is thought to underlie many diseases. A myriad of studies suggest that glutamate acts in multiple sites of the brain to regulate food intake/appetite. The majority of scientific evidence regarding the role of CNS glutamate in ingestive behavior is derived from indirect evidence from pharmacological or genetic manipulations and we still lack the analytical tools that would allow for physiologically and behaviorally relevant brain glutamate measurements. A key limitation to understanding glutamate has been its non-electroactive nature and the inability of available techniques to achieve real-time temporal resolution. Here we present a sensor design based on a carbon fiber microelectrode coated with gold nanoparticles and a monolayer of glutamate oxidase to achieve real-time glutamate detection. This in-house developed glutamate sensor was able to detect single transients of exocytotic glutamate release with temporal resolution of up to ~1 kHz *ex vivo* in rodent brain slices at the level of the nucleus accumbens. Analysis of the recorded single exocytosis indicated variability in fusion pore dynamics of glutamate release. Hence, this novel biosensor allows recording of neuronal activity in brain tissue, and offers information on the regulatory aspects of exocytotic glutamate release, which are of great importance for understanding glutamate function, and dysfunction. We now plan to apply this sensor *in vivo* to record glutamate dynamics in rats during food intake and food reinforcement tasks in select brain nuclei important in energy balance.

P76 **Validation And Behavioral Characterization Of Drd1-Icre Knock-In Rats And Adora2A-Icre Knock-In Rats**

RC DERMAN[1], JR PETTIBONE[2], E BRYDA[3], TL SAUNDERS[4,5], ED HUGHES[5], WE FILIPIAK[5], MG ZEIDLER[5], JD BERKE[2,6], CR

FERRARIO[1,7]

[1]University of Michigan, Neuroscience Graduate Program., Ann Arbor, MI, United States, [2]University of California, San Francisco, Departments of Neurology and Psychiatry., San Francisco , CA, United States, [3]University of Missouri, Department of Veterinary Pathobiology., Columbia, MO, United States, [4]University of Michigan Medical School, Department of Internal Medicine, Ann Arbor, MI, United States, [5]University of Michigan Transgenic Animal Model Core. , Ann Arbor, MI, United States, [6]University of California, San Francisco, Wheeler Center for the Neurobiology of Addiction, San Francisco , CA, United States, [7]University of Michigan, Pharmacology Department, Ann Arbor, MI, United States

The recent advent of CRISPR CAS-9 technology has enabled the development of transgenic rat models to study specific neuronal populations. Here we present data validating and characterizing recently developed transgenic rat lines in which iCre recombinase was knocked in downstream of the DRD1 or the Adora2a gene. Two rat lines were developed using CRISPR CAS-9 on a Long Evans Background: Drd1-iCre knock-in and Adora2a-iCre knock-in lines. The DRD1 gene encodes D1 dopamine receptors, thus Drd1-iCre knock-in rats should result in selective expression of Cre in D1 receptor containing neurons. The Adora2a gene codes for the adenosine A2a receptor which is highly co-localized with D2 dopamine receptors, but is absent in in tyrosine hydroxylase expressing neurons. Thus, using the Adora2a promoter should limit Cre expression to neurons with post-synaptic D2 receptors. The validation and characterization of these newly established transgenic rat models is critical to usage of these rats for studying the distinct role of D1 vs D2 expressing neurons in behavior. Here, we used genetic and immunohistochemical approaches to verify Cre expression in the correct target cells. We also verified Cre-driven viral expression of designer receptors exclusively activated by designer drugs (DREADDs) within these lines. In addition, behavioral characterization and control studies were conducted to evaluate cocaine induced locomotor activity, instrumental, and Pavlovian learning and Pavlovian-instrumental-transfer in knock-in positive and negative offspring. Finally, we examine effects of systemic Clozapine N-Oxide on these behaviors to serve as control for future studies using viral driven expression of DREADDs.

P77 **Effects Of Voluntary Wheel Running On Free-Choice High-Fat High-Sugar Diet Component Self-Selection**

JD MUL[1,2], I PIETERSE[1,2], L EGGELS[1,2], UA UNMEHOPA[1,2], K LAMUADNI[1,2], SE LA FLEUR[1,2]

[1]Department of Endocrinology & Metabolism, Academic Medical Center, Amsterdam, Netherlands, [2]Metabolism and Reward Group, Netherlands Institute for Neuroscience, Royal Netherlands Academy of Arts and Sciences, Amsterdam, Netherlands

Chronic consumption of high-caloric palatable diets (HPDs), rich in processed fats and sugars, is a major driver of the obesity epidemic, a metabolic disorder characterized by an imbalance in energy intake and expenditure. Exercise training promotes energy expenditure and induces many health benefits, including body weight- and glucose control. In both humans and rodents, exercise training alters diet choice and/or diet component preference, suggesting that changes in diet preference contribute to the exercise improvements in energy balance. Nonetheless, the underlying molecular mechanisms and the brain circuitries involved remain poorly understood. Voluntary wheel running (VWR), reinforcing rodent behavior that mimics aspects of human exercise training, is frequently used to shed light on the molecular adaptations, signaling pathways, and brain nuclei underlying the beneficial effects of exercise training on diet preference. However, such studies often utilize a two-diet [low-caloric control diet (LCD) vs. HPD] choice paradigm. To model the effects of exercise training on diet choice in humans pre-exposed to obesogenic multi-component HPDs, male Wistar rats were given access to a no-choice LCD or a free-choice high-fat high-sugar (fc-HFHS) diet, a preclinical choice diet that mimics human consumption of multi-component HPDs. Diet component preference and metabolic behavior was assessed during sedentary (baseline) and VWR conditions. Transcriptional and proteomic analysis was used to assess adaptations in hypothalamic and dopaminergic brain circuitries involved in the control of reward-driven and metabolic behavior. We will discuss our findings related to central exercise adaptations underlying altered diet preference and improvements in energy homeostasis.

P78 **Role Of Orexin-A And Dyn-A_{1-13} In The Paraventricular Hypothalamic Nucleus (Pvn) On Palatable Food Choice.**

C PEZOA, S URIBE, CE PEREZ-LEIGHTON
Department of Physiology, Pontificia Universidad Catolica de Chile, Santiago, Chile

Lateral hypothalamic orexin/dynorphin (ox/dyn) neurons co-express and co-release orexin and DYN peptides. Current data show that opioid DYN peptides and orexin-A act together to regulate reward behaviors, yet it is unclear if their interaction regulates hedonic food intake. We hypothesized that DYN-A_{1-13} and orexin-A in the PVN act together to modulate palatable food choice and intake. To test this, male Balb/c mice (N = 11) with cannulas targeting PVN, were injected into PVN with DYN-A_{1-13} (0, 0.75 nmol), orexin-A (0, 0.25 nmol) and their combination when mice had chow only or palatable foods (snacks) plus chow. When mice had only chow, DYN-A_{1-13} increased intake ($P< 0.05$) and orexin-A had no effect. When mice had chow plus snacks, DYN-A_{1-13} increased snack and chow intake, whereas orexin-A decreased snack and increased chow intake and the co-injection of these peptides had no effect on snack or chow intake ($P< 0.05$ for all effects). Next, another set of mice (N = 10) were injected bilaterally into PVN with an opioid DYN receptor antagonist (norBNI; 0, 4 ug/side) followed by orexin-A (0, 0.25, 0.5 nmol/side). NorBNI decreased only snack intake ($P< 0.05$). Orexin-A alone did not alter food intake, yet after norBNI injection orexin-A increased palatable food intake ($P=0.01$). Finally, we

made an open-source equipment to quantify feeder entry when two palatable snacks are offered. Using this device, we showed that mice spent more time in the feeder with their preferred snack. We plan to use this device to evaluate the effect of orexin-A and DYN-A_{1-13} on food choice and intake. Together, these data suggest that orexin-A and DYN-A_{1-13} have opposing effects on food choice and our new time-place sensing device may further illuminate how these peptides regulate feeding behavior.

P79 **Neuronal Sirt1 Regulates Macronutrient-Based Diet Selection Through Fgf21 And Oxytocin Signalling In Mice**

T SASAKI, S MATSUI, T KITAMURA
Institute for Molecular and Cellular Regulation, Gunma University, Maebashi, Japan

Diet affects health through ingested calories and macronutrients, and macronutrient balance affects health span. The mechanisms regulating macronutrient-based diet choices are poorly understood. What is known is that SIRT1 in part influences the health-promoting effects of caloric restriction by boosting fat use in peripheral tissues. Here, we show that neuronal SIRT1 shifts diet choice from sucrose to fat in mice, matching the peripheral metabolic shift. SIRT1-mediated suppression of simple sugar preference requires oxytocin signalling, and SIRT1 in oxytocin neurons drives this effect. The hepatokine FGF21 acts as an endocrine signal to oxytocin neurons, promoting neuronal activation and *Oxt* transcription and suppressing the simple sugar preference. SIRT1 promotes FGF21 signalling in oxytocin neurons and stimulates *Oxt* transcription through NRF2. Thus, neuronal SIRT1 contributes to the homeostatic regulation of macronutrient selection in mice and promotes pro-longevity macronutrient choices.

P80 **Food Intake In Transgenic Mice Overexpressing Mouse Apolipoprotein A-Iv**

CC LO, Z SHEN, E BINNE
Ohio University, ATHENS, OH, United States

Apolipoprotein A-IV (ApoA-IV) is one of the most abundant proteins made by the enterocytes in response to lipid intake. Exogenously intraperitoneal administration of ApoA-IV acts on vagal afferents to relay neuronal activation to the hindbrain and suppress food intake in a short-term manner. We hypothesized that transgenic mice overexpressing mouse apolipoprotein A-IV in the small intestine (ApoA-IV-Tg mice) have reduced food intake in response to feeding. *Research Design and Methods*: When ApoA-IV-Tg mice and their wild-type (WT) controls were maintained on a chow diet, meal size and food intake in animals were monitored in comprehensive lab animal monitoring system. Plasma glucose and insulin secretion in ApoA-IV-Tg mice and WT mice were determined using intraperitoneal glucose infusion. *Results:* Animals maintained on a chow diet had similar body weight and fat mass when they were maintained on a chow diet. ApoA-IV-Tg mice fed a chow diet had reduced meal size in the dark cycle and comparable total food intake. Chow-fed ApoA-IV-Tg mice had a basal glucose and insulin level comparable to that of WT mice. In addition, they had normal glucose tolerance and normal insulin response to glucose. *Conclusion:* Endogenous ApoA-IV is involved in regulating food intake in mice and is a short-term satiating protein.

P81 **Acute Amphetamine-Induced Activation Of Chemically-Identified Neurons Within The Rat Nucleus Of The Solitary Tract (Nts)**

CM EDWARDS[1], J STROTHER[2], L RINAMAN[1]
[1]Dept. Psychology, Florida State Univ., Tallahassee, FL, United States, [2]Dept. Neurosci, Univ. Pittsburgh, Pittsburgh, PA, United States

Appetite suppression is a common side effect of stimulant medications such as amphetamine, which is used clinically to treat attention-deficit/hyperactivity disorder (ADHD). The neural circuits underlying amphetamine-induced hypophagia are undescribed. The NTS receives vagal sensory signals conveying feedback about internal state, and NTS neurons project to the hypothalamus, parabrachial nucleus (PBN), and other brain regions controlling food intake, avoidance, and other motivated behaviors. Interestingly, the hypophagic effect of amphetamine is blunted in food-deprived rats, and we previously reported that food deprivation reduces stress-induced hypophagia and activation of noradrenergic and GLP-1+ neurons within the caudal NTS. To examine whether similar NTS neurons are involved in the hypophagic effects of amphetamine, we quantified neuronal activation (cFos) within the NTS in adult male Sprague-Dawley rats (n=24) treated with vehicle or amphetamine (3mg/kg, i.p.), with or without prior overnight food deprivation. Surprisingly, while amphetamine robustly activated NTS neurons, these did not include noradrenergic or GLP-1+ neurons. Instead, a small but significant number of cholecystokinin (CCK)+ neurons were activated, together with robust cFos activation within the lateral PBN, where a subset of CCK+ neurons project. There was no effect of food deprivation on NTS activation, including no effect on CCK neural activation. Our results support the view that recruitment of PBN-projecting CCK neurons may contribute to amphetamine-induced hypophagia.

P82 **Central Oxytocin Receptor Signaling Bidirectionally Effects Social Transmission Of Food Preference In Rats Based On Conspecific Familiarity.**

CM LIU, VW LEE, EE NOBLE, AN SUAREZ, SE KANOSKI
University of Southern California, Los Angeles, CA, United States

Oxytocin potently reduces food intake following either peripheral or central administration, however, its role in conditioned aspects of feeding behavior remains largely unexplored. Based on the established role of oxytocin in promoting social behaviors, we utilized a rodent behavioral procedure known as 'social transmission of food preference' (STFP) to examine the effects of central oxytocin signaling in conditioned social aspects of feeding. In this task, 'observer' rats learn to prefer a flavored chow based on a social interaction with another 'demonstrator' rat that recently consumed the flavored chow. Control observer rats given lateral intracerebroventricular (ICV) vehicle injections immediately prior to the social interaction preferred the demonstrator-paired flavored chow vs. novel flavored chow in a preference test given 24hr after the interaction, whereas STFP was significantly reduced by ICV oxytocin (1ug) injections given prior to the interaction. These results were surprising given that oxytocin is known to promote social behaviors. We hypothesized that these unexpected findings may be based on conspecific familiarity, as demonstrator and observer rats were only briefly habituated to each other prior to the interaction. In a follow-up study, demonstrators and observers were given 4 social interaction sessions in an enriched environment prior to the STFP procedure. Results reveal that under these conditions ICV administration of oxytocin significantly increased preference for the demonstrator-paired flavor relative to controls, suggesting that oxytocin effects on STFP may be based on "in-group favoritism". Future studies are needed to characterize the neural pathways through which oxytocin bidirectionally influences conditioned social aspects of feeding.

P83 **Leptin Targets Lateral Hypothalamic And Ventral Tegmental Gabaergic Neurons To Reduce Dopaminergic Drive Towards Food Reward**

RAH ADAN[1,2], A OMRANI[1], V DE VRIND[1]

[1]Brain Center Rudolf Magnus, Utrecht, Netherlands, [2]Sahlgrenska Academy, Gothenburg, Sweden

Leptin reduces motivation to obtain food rewards when in negative energy balance. Although leptin directly reduces activity of ventral tegmental (VTA) dopamine neurons, most of these dopamine neurons do not project to the accumbens which is the dopamine projection implicated in driving food reward seeking. It has been proposed that leptin-receptor expressing GABA neurons in the lateral hypothalamus (LH) mediate leptin's effect on dopaminergic activity, either directly by projecting to the VTA, or via orexin neurons projecting to VTA dopamine neurons. Using optogenetics-assisted circuit mapping in leptin receptor cre mice, we find that LH GABAergic neurons project to VTA neurons. Leptin inhibits the activity of these neurons. Chemogenetic activation of these LH neurons increased the motivation to press lever to obtain a sucrose reward. We also find that VTA GABA neurons expressing leptin receptors project onto VTA dopamine neurons. Activation of leptin receptor expressing neurons in the VTA using chemogenetics reduced the motivation to press lever for a sucrose. Thus, in the VTA leptin receptor expressing GABA neurons are more important than leptin receptor expressing dopamine neurons in mediating the effect of leptin on reducing motivation for food reward. We conclude that leptin indirectly targets multiple inputs to the dopamine system to reduce food reward seeking.

P84 **Characterization Of A Novel Glutamatergic Pathway Linking Feeding And Reward Centers Of The Brain**

AE SMITH[1,2], DL MCCUE[1,2], JM KASPER[2,3], J PERIS[4], JD HOMMEL[2,3]

[1]Department of Neuroscience, Cell Biology, and Anatomy, University of Texas Medical Branch, Galveston, TX, United States, [2]Center for Addiction Research, University of Texas Medical Branch, Galveston, TX, United States, [3]Department of Pharmacology, University of Texas Medical Branch, Galveston, TX, United States, [4]Department of Pharmacodynamics, University of Florida, Gainesville, FL, United States

Obesity affects 37.5 percent of the adult population in the United States. Pharmacotherapies for obesity have limited efficacy, often resulting in 5% weight loss or less. Obesity is caused, in part, by chronic overconsumption of high-fat food. High-fat food is extremely motivating, and overconsumption of high-fat food resembles addiction-like behavior, a phenomenon described as the addictive dimensionality of obesity. The neurobiological aspects of motivation for high-fat food remain underexplored, and represent an opportunity to identify novel neurocircuits. One such neurocircuit involves the paraventricular nucleus of the hypothalamus (PVN), which has projections to the nucleus accumbens (NAc). Currently, the role of PVN->NAc in motivation for high-fat food is not known. The goal of these studies was to determine the structural, functional and behavioral significance of the PVN-> NAc circuit on motivation for high-fat food. We used immunohistochemistry to demonstrate that PVN-> NAc neurons co-localize with VGLUT, suggesting glutamtergic signaling. To characterize PVN-> NAc neurotransmission, we used an excitatory DREADD. Neurotransmitter release was quantified by microdialysis, and activation of PVN-> NAc induced glutamate release. We also used DREADDs to investigate behavioral implications of PVN-> NAc activation on motivation for high-fat food. DREADD-mediated activation of PVN-> NAc decreased lever pressing on a progressive ratio schedule of reinforcement for high-fat food reinforcers compared to control, which is consistent with increased glutamate release. Thus, the PVN-> NAc circuit regulates motivation for high-fat food, and could represent a novel mechanism involved in the addictive dimensionality of obesity.

P85 **Role Of The Supramammillary Nucleus In Ingestive And Motivated Behavior.**

L LóPEZ-FERRERAS[1], KK EEROLA[1], JE RICHARD[1], OT SHEVCHOUK[1], FH NILSSON[1], MR HAYES[2], KP SKIBICKA[1,3]

[1]Institute for Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden, [2]Department of Psychiatry, University of Pennsylvania,

Philadelphia, PA, United States, [3]Wallenberg Centre for molecular and translational medicine, University of Gothenburg, Gothenburg, Sweden

The supramammillary nucleus (SuM), located dorsal to the mammillary region and immediately caudal to the hypothalamus, is characterized by dense bidirectional connections with most hypothalamic and septal nuclei. This neuroanatomical position points to a potential of this nucleus to regulate ingestive and motivated behavior. Yet, very few studies, if any, focus on the SuM. Here we investigate the role of SuM GLP-1 receptors in regulation of ingestive and motivated behavior in male and female rats. This pursuit was supported by previous data indicating this is a GLP-1 peptide binding site. While GLP-1 analogue, exendin-4, microinjections directly into the SuM reduced chow, high-fat, or sugar intakes in both male and female rats, food-motivated behavior, measured by the sucrose motivated operant conditioning test, was only reduced in male rats. This contrasted with the results obtained from the neighboring structure, the ventral tegmental area, where females displayed a more potent response to GLP-1R activation by exendin-4. Considering our recent results indicating unparalleled hyperphagia, weight, and fat gain after GLP-1R knockdown in LH, along with the fact that SuM is sometimes considered a caudal extension of the LH, we next knocked down GLP-1R in the Sum. Surprisingly, and in contrast to the LH results, SuM GLP-1R knockdown did not alter food intake, body weight or food motivation in lean or obese, female or male rats. These results indicate the potential for SuM to contribute to ingestive and motivated behavior regulation, that can be sex divergent, depending on the behavior of interest. They also extend the map of brain sites directly responsive to GLP-1 agonists.

P86 **Investigating The Neuroendocrine And Behavioral Controls Of Cannabis-Induced Feeding Behavior.**

JF DAVIS, PQ CHOI, J KUNZE, P WAHL
Washington State University, Pullman, WA, United States

Cannabis induces appetite, but little is known regarding its mechanistic control of feeding behavior. Previous studies have examined delta-9 tetrahydrocannabinol (THC), the primary psychoactive cannabinoid in cannabis, for its appetite-stimulating effects. However, few have investigated feeding following dry cannabis plant matter (CPM) exposure, the most widely consumed form of cannabis. Clinical data report that CPM-induced feeding only ensues after a time delay, suggesting additional signaling mechanisms beyond THC action. To address this, we utilized a novel vapor chamber system to administer CPM to rodents. Specifically ad libitum male Long Evans rats (n=8/group) were exposed to vaporized CPM and meal patterns were subsequently analyzed. Plasma levels of THC and the orexigenic hormone acyl-ghrelin (AG) were also quantified. Another cohort of 24hr deprived male rats (n=8/group) received CPM exposure following a 2hr re-feeding period prior to palatable ensure diet exposure. Additional rats were evaluated for CPM-induced feeding following pharmacologic blockade of AG secretion. Finally, experiments to measure motivated and anxiety-driven behavior following CPM exposure were performed. Results indicate that CPM exposure induced a delayed increase in meal frequency, an effect accompanied by elevated levels of plasma ghrelin and THC. CPM exposure also augmented ensure feeding in pre-fed rodents. CPM exposure did not alter motivated or anxiety-driven behavior. Importantly, blockade of AG secretion attenuated CPM-induced feeding. Collectively these data indicate that vaporized CPM stimulates feeding occurs in a time dependent manner and requires gastrointestinal release of AG.

P87 **Mechanisms Underlying Different Behavioral Forms Of Cue-Potentiated Feeding**

LM RAYCRAFT[1], NM RUSSELL[1], AW JOHNSON[1,2]
[1]Department of Psychology, Michigan State University, East Lansing, MI, United States, [2]Neuroscience Program, Michigan State University, East Lansing, MI, United States

Cue-potentiated feeding (CPF) provides the opportunity to study the influence of food associated cues on overeating behaviors. Typically, in these studies a conditioned stimulus (CS+) signals the delivery of an appetitive unconditioned stimulus (US)—when subsequently tested under sated conditions, a significant increase in overeating of the US is observed during CS+ presentations. While CPF has been demonstrated in a variety of experimental settings, the precise parameters underlying its expression remain relatively unknown. In the current study, we examined whether during training varying the density of US delivery (Experiment 1) or CS-US interval (Experiment 2) would reveal different behavioral forms of CPF. In Experiment 1, mice received presentations of a 20 s auditory CS+ which predicted the delivery of a sucrose US at a density of 1/9s (Group-20-s). A second group of mice received a 120 s auditory CS+ during which the US was delivered at a density of 1/49 s (Group-120-s). While all mice showed CPF at test, Group-20-s mice displayed higher CS+ evoked lick rates. In addition, an analysis of licking microstructure revealed that Group-120-s mice displayed CS+ evoked licking behavior that reflected an increase in the perceived palatability of the sucrose US. In Experiment 2, mice were trained with a CS-US interval of either 9 s or 49 s. During testing, only mice trained with the 49 s CS-US interval displayed cue-potentiated feeding. These results are discussed with respect to the influence of US density and CS-US interval on associatively activated sensory and affective representations of a US, contrast mediated effects resulting from presentation of excitatory and inhibitory CSs, and implications for feeding and obesity.

P88 **Behavioral And Biological Support To The Binge Eating Prone And Resistant Profiles**

L BEKKER[1,4], L MOSHE[1,2], T KISLIOUK[3], N MEIRI[3], A WELLER[1,2]
[1]Gonda Brain Research Center, Bar Ilan University,, Ramat Gan,, Israel, [2]Psychology Department, Bar Ilan University, Ramat Gan,, Israel, [3]Institute

of Animal Science, ARO, The Volcani Center, Bet Dagan, Israel, [4]University of Haifa, Haifa, Israel

A well establish Binge eating animal model claimed that we can identify rats that are binge eating prone (BEP) and rats that are binge eating resistant (BER). The aims of the present study were to see if these profiles differ behaviorally toward palatable food and if we can find biological biomarkers that distinguish between BEP and BER rats. Methods:Project 1: Wistar BEP and BER rats received lactose that causes them abdominal discomfort, when eating Oreo cookies, to test their motivation to obtain Oreo. Project 2: Obese OLETF and normal weight LETO rats were first divided to BEP and BER. Tissue punches of the ventral tegmental area (VTA) and of the hypothalamic arcuate nucleus (ARC) were taken. Gene expression was measured by quantitative RT-PCR. Results:Project 1: BEP rats showed high motivation to obtain a large amount of preferred diet even when this predictably was followed by abdominal discomfort caused by lactose ingestion. Project 2: We found that obese OLETF rats are more BEP compared to LETO controls. In addition, only in the control LETO rats, gene expression in the VTA was correlated to binge size and in the ARC to body weight gain. OLETF-LETO differences in gene expression were also found. In this study, we showed that BEP rats showed pathological motivation for food. In addition, we showed that obese OLETF rats are at higher risk to develop binge eating than controls. Finally, different brain areas are differently associated with binge eating and overweight.

P89 **Reward Sensitivity, Grazing, Food Addiction, And Snacking While Viewing Television With Embedded &Ldquo;Fast Food&Rdquo; Advertisements**

NJ LOXTON, JM TAYLOR
Griffith University, Brisbane, Australia

External food cues, such as fast food advertisements, have been found to influence eating behaviour. Individual differences in reward sensitivity have been related to noticing and responding to such cues. Previous research found exposure to fast food advertisements increased urge to eat, and subsequent snack food consumed, in participants high in reward sensitivity. Following from this research, the aim of this study was to investigate the association between reward sensitivity and food consumption while viewing a television show with, and without, fast food advertisements. Associations with other forms of overeating: grazing (repetitive snacking over an extended period) and food addiction symptoms (excessive over-consumption) were also assessed. 100 undergraduate students (66% female) were randomly exposed to fast-food advertisements or non-food advertisements embedded within a 30-minute movie. Participants were allowed to snack on chocolates while they viewed the movie in a controlled laboratory. Reward sensitivity, food addiction, and grazing were measured with established self-report questionnaires. Cue condition moderated the association between reward sensitivity and food consumed ($B = 1.62$; $p = .03$) - heightened reward sensitivity was associated with amount of food consumed during the movie, but only for participants exposed to food cues (food cue $r = .30$, $p = .03$, no food cue $r = -.18$, $p = .25$). Reward sensitivity was also significantly associated with grazing ($r = .33$, $p = .001$) and food addiction symptom count ($r = .41$, $p < .001$). These findings provide further support that those with heightened reward sensitivity are particularly susceptible to the influence of food cues, which may influence overeating and related behaviours.

P90 **Attentional Bias For Food Cues In Advertising Among Children With Overweight And Hunger: A Randomized Controlled Trial.**

F FOLKVORD[1,2,3], D.J. ANSCHUTZ[1], M. BUIJZEN[1]
[1]From the Behavioural Science Institute BSI, Communication Science, Radboud University, Nijmegen, Netherlands, [2]From the Applied Social Science and Behavioural Economics research group, Universitat Oberta de Catalunya, Barcelona, Spain, [3]From Communication Science, Amsterdam University, Amsterdam, Netherlands

Attentional bias theory suggests that people with an increased motivation to receive or avoid a rewarding substance show increased automatic selective attention towards cues that are related to that specific substance. The aim of this study was to examine if children with overweight and hunger have an attentional bias for food cues when exposed to food advertising. A randomized between-subject design (RCT) was used with 95 children who played an advergame that promoted either energy-dense snacks or nonfood products. While playing, duration of fixation, number of fixations, and latency of initial fixation to food or nonfood cues were recorded. Children with overweight had a higher gaze duration for the food cues compared to normal weight children. No effects were found of overweight on the attentional bias measurements for the nonfood cues. Furthermore, hungrier children had a higher gaze duration, a higher number of fixations, and a faster latency of initial fixation on the food cues than less hungry children, while we found the opposite results for the nonfood cues. The findings largely confirm our expectations, adding important knowledge to existing literature about the individual susceptibility to food advertisements.

P91 **Compulsive &Lsquo;Grazing&Rsquo; And Addictive Tendencies Towards Palatable Foods**

R BONDER[1], C DAVIS[1], JL KUK[1], N LOXTON[2]
[1]York University, Toronto, ON, Canada, [2]Griffith University, Queensland, Australia

Excessive consumption is a hallmark characteristic of any substance-use disorder. To date, research in the field of *food addiction* has focused largely on binge eating as a key symptom of this syndrome. The current study is the first to investigate other patterns of overeating in those who display addictive tendencies towards food – most importantly compulsive grazing, a behavior identified as a frequent post-operative outcome of bariatric surgery. Adult men and women between the ages of 20 to 50 years (n=222) were recruited for this laboratory-based study. Participants completed self-report questionnaires including eating-behavior measures and related personality measures, which served as covariates in the analysis. Height and weight were measured, and demographic questions were administered via interview. Multiple regression analysis was employed using the *Yale Food Addiction Scale* (YFAS) as the dependent variable. Results indicated that addictive personality traits (p=0.008), loss-of-control eating (p< 0.0001), and compulsive grazing (p=0.003) each contributed unique variance to the YFAS score (R^2=0.61, F(8,207)=41.49, p< 0.0001). Surprisingly, binge eating did not reach statistical significance. These findings provide novel insight into the association between a grazing pattern of overeating and food addiction, and further validate its similarity to traditional addiction disorders such as alcoholism, where continual consumption throughout the day may also be a characteristic pattern of intake.

P92 **Obesity And Neurofeedback: A Single-Blind Randomized Controlled Trial To Improve Food-Related Behavior By Activation Of Self Control Related Brain Areas**

R VEIT[1,2], SH KOHL[1,3], S KULLMANN[2], MS SPETTER[1,4], A RINA[1,5], N BIRBAUMER[1], M HALLSCHMID[1,2], H PREISSL[2]

[1]Institute of Medical Psychology and Behavioral Neurobiology, University of Tübingen, Tübingen, Germany, [2]Institute for Diabetes Research and Metabolic Diseases, Tübingen, Germany, [3]Institute of Neuroscience and Medicine, Forschungszentrum Jülich, Jülich, Germany, [4]School of Psychology, University of Birmingham , Birmingham, United Kingdom, [5]Southern Jamaica Plain Health, Harvard Medical School , Boston, MA, United States

Obese individuals show alterations in inhibitory control and associated prefrontal function in response to food items. The dorsolateral prefrontal cortex (dlPFC), which shows reduced activation in obese subjects, is specifically related to self-control and, apparently, dietary success. In the present study we investigated the impact of volitional up-regulation of dorsolateral prefrontal cortex (dlPFC) activity via fMRI neurofeedback training in obesity. Thirty-eight overweight or obese subjects (BMI, 25-40 kg/m²) took part in a randomized controlled trial. During fMRI neurofeedback, participants either had to increase activity of the left dlPFC or visual cortex. The training session took place on a single day and included three training runs of six trials of up-regulation and passive viewing. Food appraisal were assessed before and after training and in a follow-up session. Participants in both groups upregulated activity in the targeted brain area successfully. However, participants of the control group also showed dlPFC activation during up-regulation reported higher expectations towards the neurofeedback training. At follow-up, both groups rated pictures of high-, but not low-calorie foods as less palatable and chose them less frequently compared to the baseline. Actual snack intake remained unchanged, but sweet snacks were rated less tasty during follow-up. We show that fMRI neurofeedback training enables individuals with obesity to up-regulate activity of the left dlPFC. Behavioral training effects were observed in both groups, which might be explained by dlPFC co-activation and psychosocial factors in the control group. Neurofeedback training of dlPFC activity might therefore support therapeutic strategies aiming at improved self-control in obesity.

P93 **Prefrontal Cortex Activation Predicts** Food-Specific Impulsive Behavior

S KULLMANN[1], K SCHAG[2], R VEIT[1], M BORUTTA[1], S ZIPFEL[2], K GIEL[2], H PREISSL[1]

[1]Institute for Diabetes Research and Metabolic Diseases, University of Tübingen, Tübingen, Germany, [2]Department of Psychosomatic Medicine and Psychotherapy, University Hospital Tübingen, Tübingen, Germany

Behavioral and cognitive control of eating behavior are vital for healthy food choices. We investigated the frontal network during response inhibition (food specific go/no-go task) using near-infrared spectroscopy (NIRS) in patients with binge eating disorder (BED) and healthy controls. NIRS is a non-invasive method comparable to fMRI without restriction of the tight bore, which makes it difficult to measure morbidly obese individuals with MRI. Currently no study applied functional NIRS measurements from cortical regions as predictors of eating behavior relevant measures. We recruited 12 healthy controls (BMI range 20.9-27 kg/m^2) and 25 BED patients (BMI range 22.6-59.7 kg/m^2). As previously reported, we found a significant response inhibition effect, resulting in increased oxygenated hemoglobin response in prefrontal cortex (PFC) in both groups. Moreover, BED patients showed a much weaker activation of the dorsolateral PFC during response inhibition than healthy controls, predominantly in the right hemisphere. Interestingly, hypoactivity of the PFC was related to trait impulsivity of the BED patients. Higher impulsivity scores, especially motor impulsivity, predicted lower DLPFC activation during response inhibition. Overall, we were able to show that fNIRS measurements during response inhibition can be successfully assessed in lean, overweight and morbidly obese individuals.

P94 **Identifying Determinants Of Loss Of Control Of Eating In Children Using Association Rules Data Mining**

AL PEARCE[1], LK ENGLISH[1], M TANOFSKY-KRAFF[2], KL KELLER[1]

[1]Pennsylvania State University, State College, PA, United States, [2]Uniformed Services University, Bethesda, MD, United States

Loss of control (LOC) eating in children is associated with increased risk for binge eating disorder and the development of obesity. However, the determinants of LOC in childhood remain unclear. Association rules mining (ARM), a data-driven technique that identifies frequent and causal structures in data, was used to generate hypotheses and identify potential targets for interventions to prevent obesity. We conducted secondary analysis of data compiled from five prior studies that included child-reported LOC (via interview; 23%, n=37), parent-reported child appetite traits and feeding practices, and body composition for 162 (F=93) children (7-12 y; M: 9.4, SD: 1.4). ARM was conducted with accepted minimum thresholds for the identification of rules, which consist of sets of items that predict LOC. The resulting 150 rules were ranked on specificity for predicting LOC, resulting in 9 rules. Exclusive breast feeding < 7 mo and high food fussiness were predictors in 8 rules. Low parent-reported pressure to eat was a predictor in 6 rules. Child characteristics (i.e., age and sex), parent education, and income were not identified in any rules. Hierarchical clustering identified two groups of rules: one group had predictors related to high food responsiveness and the other had predictors related to high desire to drink. Additionally, the second group of rules had more predictors related to high child fat-mass index and father weight status (BMI >= 25 kg/m^2). Together these results indicate that feeding practices, appetite traits, and child/father body composition may be predictive of LOC in children and provide an example for the utility of data mining in identifying targets for experimental work.

P95 **Acute Nutritional State And Body Mass Index Influence Anterior Cingulate Cortex Activation During Motor Response Inhibition**

EF ROELOFS[1], LJ NESTOR[1], SN ALI[2], AR LINGFORD-HUGHES[1], DJ NUTT[1], AP GOLDSTONE[1]

[1]PsychoNeuroEndocrinology Research Group, Neuropsychopharmacology Unit, Centre for Psychiatry, Division of Brain Sciences, Imperial College London, Hammersmith Hospital, London, United Kingdom, [2]Department of Endocrinology and Diabetes, Royal Free London NHS Foundation Trust, London, United Kingdom

Acute and chronic changes in nutritional state influence eating and addictive behaviours that may promote over-eating, including impulsivity and compulsivity. Altered activation in networks involved in motor inhibitory control has been reported in obesity. The influence of acute changes in nutritional state, like fasting, on neural correlates of motor inhibitory control are uncertain. We examined this using a functional MRI non-food related Go-NoGo task, completed by twenty-one healthy, non-obese adults, after an overnight fast (Fasted) or 90 minutes after a fixed 1200 kcal liquid meal (Fed), in a cross-over design. Participants had significantly greater blood oxygen level dependent (BOLD) signal during successful motor response inhibition (NoGo correct inhibition > Go baseline), when Fasted than when Fed, in the right anterior cingulate cortex (ACC) and right insula, despite similar task accuracy. Furthermore, BMI was negatively correlated with ACC BOLD signal during successful motor response inhibition, and positively with task accuracy. These results suggest that fasting requires enhanced ACC/insula engagement to achieve successful motor response inhibition; while obesity is associated with less ACC engagement coincident with enhanced accuracy during motor response inhibition, at least to non-food related stimuli. Thus, both acute and chronic nutritional state may impact on neural circuits involved in motor response inhibition.

P96 **Altered Functional Connectivity In Individuals With Loss Of Control Eating.**

L BENSON, K OSIPOWICZ, F ZHANG, MR LOWE
Drexel University, Philadelphia, PA, United States

Eating disorders (ED) are difficult to treat. A better understanding of ED etiology would help inform treatment and prevention. Loss of control eating (LOC), a sense of not being able to stop or control eating, accompanies binge eating in individuals with bulimia nervosa or binge eating disorder. Additionally, LOC can be an early marker of eating-related psychopathology in children. Few studies have examined brain network alterations related to LOC. A better understanding of the early neural-behavioral correlates of ED symptoms can help identify who might be at risk of future disease development or increased severity. This study examined whole brain functional connectivity using resting state fMRI in individuals with LOC. The sample included male and female individuals who did (n=49) or did not (n=49) endorse LOC (matched for age and gender), assessed by a yes/no response to the diagnostic question, “Has there been a time when your eating was out of control?” Participants were aged 10-20 years and part of the 1445 Philadelphia Neurodevelopmental Cohort that underwent neuroimaging. Individuals reporting LOC (vs. no LOC) demonstrated disturbances in resting state functional connectivity between frontoparietal regions and regions associated with the default mode network, visual processing (e.g. occipital gyrus), and appetitive behavior (e.g. frontal operculum). These findings are consistent with the idea that individuals with LOC have dysfunction of self-regulation over their intrinsic state and sensory processing. These findings provide first insights into the neural basis of LOC individuals’ difficulty controlling appetitive drive and their poor control and distorted perceptions of the state of their body; traits that often characterize individuals with ED.

P97 **Corticosterone Rapidly Inhibits Vagal Afferent To Nts Signaling Via Cannabinoid Subtype 1 Receptors.**

FJ SHAFFER, JEM LINDBERG, M SAVENKOVA, IN KARATSOREOS, JH PETERS
Washington State University, Pullman, WA, United States

Centrally, vagal afferent terminals release the excitatory neurotransmitter glutamate (GLU) onto neurons in the nucleus of the solitary tract (NTS) and integrate direct gastrointestinal signals with ongoing NTS activity and circulating hormones. Glucocorticoid levels increase rapidly in response to stress, fasting, as well as exhibit a diurnal rhythm; all conditions that impact feeding. In this project we investigated the rapid, membrane delimited effects of corticosterone on GLU signaling in the NTS using patch-clamp electrophysiology on acute brainstem slice preparations containing the NTS and central vagal afferent terminals. Brainstem slices were isolated from adult male C57BL/6 mice and recorded for 3-4 hours following isolation. We found that bath application of CORT rapidly suppressed presynaptic GLU release onto NTS neurons. We observed a large decrease in the frequency of spontaneous release as well as an inhibition of action-potential evoked release. The effect of CORT was blocked by mifepristone and phenocopied by dexamethasone, consistent with rapid glucocorticoid receptor (GR) mediated signaling. To elucidate a potential mechanism of these fast effects, we investigated the contribution of the retrograde endocannabinoid (eCB) signaling system, which has been reported to transduce non-genomic GR signals. Pharmacological blockade of the cannabinoid type 1 (CB1) receptor (AM251 or AM4113) blocked CORT induced suppression of GLU release, as did genetic deletion of CB1 receptors. These results demonstrate spontaneous and evoked GLU release in the NTS can be rapidly controlled by the GR via retrograde eCB signaling. This provides a plausible mechanism whereby the NTS may integrate circulating endocrine signals with fast neurotransmission to control food intake.

P98 **Sleep Disruption Modifies Preference For Hedonic Foods In Rats Fed A Cafeteria Diet**

J YU[1], MM HOUSER[2], CE PEREZ-LEIGHTON[3,4], JA TESKE[1,2,4,5]

[1]Department of Nutritional Sciences, University of Arizona , Tucson, AZ, United States, [2]Physiological Sciences Graduate Interdisciplinary Program, University of Arizona, Tucson, AZ, United States, [3]Departamento de Fisiologia, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile, Santiago, Chile, [4]Department of Food Science & Nutrition, University of Minnesota, Saint Paul, MN, United States, [5]Minnesota Obesity Center, Saint Paul, MN, United States

Our environment provides easy access to hedonic foods. Environmental noise alters sleep, food preference and promotes excessive eating and obesity. We showed that sleep disruption (SD) due to environmental noise increased weight gain and non-hedonic food intake in rats. Sodium oxybate (SXB), an FDA-approved sleep medication, may reduce eating and obesity due to poor sleep. Yet, it's unclear if access to a hedonic diet modulates the effects of SD or SXB on preference, intake or weight gain. Male Sprague-Dawley rats (N=67) were fed chow or cafeteria diet (CAF-D, 24 hedonic foods) for 7d followed by 9d with or without SD (8h/d) and saline or SXB (500mg/kg, i.p. daily). The CAF-D significantly increased weight gain and calorie intake compared to chow, while CAF-D+SD significantly increased weight gain and intake relative to CAF-D or SD alone (all comparisons $P < 0.05$). Changes in CAF-D food preference patterns were analyzed with compositional analysis using the Kullback-Liebler distance (KLD) to represent the relative distribution of calories from individual CAF-D foods. First, comparisons with random models showed that existing preferences became more defined during treatment only for rats that slept undisturbed ($P < 0.03$). Second, analysis of the robustness of preferences between acclimation and treatment indicated a significant interaction between sleep and SXB ($P = 0.003$) and KLD was significantly lower in SD rats independent of SXB compared to saline-treated rats that slept undisturbed ($P < 0.05$). Thus, the anorectic effect of SXB occurs without altering food preference, while hyperphagia due to SD prevents food preference from becoming more defined, suggesting that CAF-D and SD increase weight gain by elevating intake of preferred and non-preferred foods equally.

P99 **A Novel Projection From The Paraventricular Hypothalamus That Underlies Emotional Control Of Feeding**

Q TONG[1,2,6], Y XU[1], Y LU[1], LR MANGEIRI[1,2], RM CASSIDY[1,2], Y XU[3], BR ARENKIEL[4,5]

[1]Institute of Molecular Medicine McGovern Medical School UTHealth, Houston, TX, United States, [2]MD Anderson UTHealth Graduate School of Biomedical Sciences, Houston, TX, United States, [3]CNRC and Department of Pediatrics, Baylor College of Medicine, Houston, TX, United States, [4]Department of Molecular and Human Genetics, and Neuroscience, Baylor College of Medicine, Houston, TX, United States, [5]Jan Duncan Neurological Research Institute, Texas Children's Hospital, Houston, TX, United States, [6]Department of Neurobiology and Anatomy, Houston, TX, United States

Feeding is known to be profoundly influenced by emotional status with unclear neural basis. Functional projections from the paraventricular hypothalamus (PVH), a known feeding center, to the telencephlon have not been demonstrated. Here, we identify a direct projection from PVH to the ventral part of lateral septum (LSv). Optogenetic activation of PVH→LSv terminals produces a scalable effect on feeding inhibition and aversion associated with self-grooming (weak aversion) and frantic escape jumping (strong aversion). The aversion is blocked by either disrupting glutamate release or inhibiting glutamate receptors in LSV while inhibiting PVH→LSv terminals or LSv glutamate receptors increases feeding. PVH and LSV neurons are activated by water-spray induced self-grooming and conspecific attacking. Thus, the PVH neurons underscores emotional control of feeding through direct glutamatergic projections to the LSv.

P100 **Sex Differences In Food Consumption Under Novelty**

E.M. GREINER, G.D. PETROVICH
Boston College, Chestnut Hill, MA, United States

Novel foods and novel environments impact consumption, but how the two interact, and whether there are sex differences, is less known. Here, we sought to determine if exposure to a novel context enhances neophobia to a novel food, and whether the effect is sex dependent. Male and female Long Evans rats were tested for consumption in either their home cage or in a novel context (n=8 per group) and were given two foods, one familiar (rat chow) and one novel (Test Diet pellets; TD). They received 8 testing sessions on separate days and were food deprived (20 hours) prior to each. During Test 1 and 2, males and females tested at home consumed significantly more rat chow than TD ($p=0.001$, both) while rats tested in a novel context ate similar, small amounts of each food. Total consumption was lower in the novel context groups compared to home for both sexes ($p=0.002$, both) but females tested in the novel context ate the least. In Test 3, male and female rats tested at home consumed equal amounts of the two foods and by Test 8 were consuming significantly more TD (males, $p=0.03$; females, $p=0.016$). Novel context tested males showed preference for TD by Test 4 ($p=0.014$) whereas females showed equal consumption of both foods during all tests. Further analysis of total consumption in Test 6, 7, and 8 showed that novel context tested males ate significantly more than females (T6, $p=0.009$; T7, $p=0.008$; T8, $p=0.003$). These results indicate that rats in a familiar context, regardless of sex, and males in a novel context habituate to novelty faster than females in a novel context, that showed sustained, suppressed consumption throughout testing.

P101 **Effects Of Individual Versus Social Housing On Energy Balance And Metabolic Health In Rodents**

G VAN DIJK[1], L HARVEY[2], E VAN DER BEEK[2,3], G KARAPETSAS[2], S VAN HEIJNINGEN[2], AL SCHIPPER[1,2]

[1]Groningen Institute for Evolutionary Life Sciences (GELIFES), Neurobiology Cluster, Department Behavioral Neurosciences, University of Groningen, Groningen, Netherlands, [2]DANONE Nutricia research, Utrecht, Netherlands, [3]Department of Pediatrics, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands

Evidence for potential long-term consequences of individual (IND) versus social (SOC) housing on body weight homeostasis, energy balance and metabolic phenotype is inconsistent. For this reason, we performed a systematic review and meta-analysis, which included a total of 71 rat or mouse studies of similar sexes to compare these effects. We did not find a main effect of IND versus SOC housing on body weight. In sub-stratifications, however, both food intake and visceral adipose tissue mass were significantly higher in IND versus SOC housed animals irrespective of animal type, sex, or diet. We further tested these outcomes experimentally in male C57Bl6/J mice that were housed at 21^{o}C either living IND or living in couples (CPL), and either exposed to a low fat (LF) or a high fat (HF) diet. We observed that IND mice had higher visceral and subcutaneous fat mass than CPL mice, and this was most outspoken in the HF diet condition. Relative to CPL mice, IND mice had increased energy intake irrespective of diet, and resting energy expenditure was also increased. IND housed mice also had increased interscapular BAT UCP-1 expression specifically in those feeding HF diet. Surprisingly, IND mice showed more entries and time spent in open versus closed arm in an elevated plus maze test, had a higher attention to mice in a social approach test, and had lower plasma corticosterone levels compared to CPL mice. These data indicate that IND mice have profound behavioral and metabolic alterations probably due to lack of social thermoregulation, but have less emotional stress than CPL mice. Latter outcomes may be biased because of the fact that psychological assessments frequently require animals to be tested alone, which is a novel situation for CPL, but not for IND mice.

P102 **Predictors Of Stress-Induced Eating Differ For Women Displaying Stress Over-Eating Versus Under-Eating**

RR KLATZKIN[1], HR KISSILEFF[2], C CATTANEO[1], R DASANI[1], M WARREN[1], T NADEL[1]

[1]Rhodes College, Memphis, TN, United States, [2]Columbia University Medical Center, New York , NY, United States

Acute stress can lead to over-eating for some individuals, and under-eating for others. According to the individual difference model, factors such as obesity, stress responsivity, and eating styles can influence stress-induced hypo- or hyper-phagia; however, what is not yet understood is whether the factors that predict stress-induced eating are different for those who over- versus under-eat post-stress. Individual differences in the psychophysiological factors that drive stress-induced eating may lead to the development of these dichotomous behaviors. In order to assess the influence of emotional eating, negative affect, subjective stress, hunger, cardiovascular reactivity, and BMI on stress-induced eating, 27 undergraduate women (ages 17-22; mean = 19; BMIs 18-37, mean = 22) were given snacks (chips, golden oreos, and M&Ms) to eat after a mental stress task (Trier Social Stress Test) or a rest period. Women were classified as displaying either stress-induced hyper-phagia (n = 13) or hypo-phagia (n = 14) based on the difference in the amount of snack food eaten following stress or rest. For women displaying stress-induced hypo-phagia, hunger ($r = 0.81$, $p = .000$), and stress-induced systolic blood pressure (BP; $r = 0.52$, $p = .055$), diastolic BP ($r = 0.61$, $p = .02$), and heart rate ($r = 0.55$, $p = .04$) predicted stress-induced snack intake. For women displaying hyper-phagia, BMI predicted stress-induced snack intake ($r = 0.88$, $p = .000$). None of the factors differed between groups. Thus, different psychophysiological factors may drive stress-induced snacking for women displaying hypo- versus hyper-phagia, although further physiological measures such as cortisol should also be explored.

P103 **The Secondary Functions Of Appetite: The Stimulation Of Appetite By Insecurities In Non-Food Resources Relevant For Survival And Advancement**

BK CHEON[1, 2]

[1]School of Social Sciences, Nanyang Technological University, Singapore, Singapore, [2]Clinical Nutrition Research Centre, Singapore Institute for Clinical Sciences, A*STAR, Singapore, Singapore

While hunger is conventionally perceived as a product of energy/nutrient deprivation, growing research suggests that appetite may also be stimulated by other forms of deprivation. Here, I propose a potential secondary adaptive function of the systems regulating appetite to more broadly monitor and correct perceived deficiencies in resources necessary for advancement, survival, and reproduction. This framework proposes that across species, the basic need to monitor critical resources for survival beyond nourishment, such as territory and social standing (and material/symbolic resources for humans), may have involved an adaptive co-opting or extension of the psychological and physiological architecture of the appetite regulation system to also be sensitive to perceived insecurities in these essential non-food resources. Consequently, deprivation of these resources may also co-activate appetite and promote behaviors that risk increased energy intake and obesity. I will provide support for this framework from four experimental studies which demonstrate that insecurities and perceived inadequacies of socioeconomic resources (which are critical for survival and advancement among humans) produce selection of larger portion sizes (Study 1), increased energy intake (Study 2), and elevated circulation of an orexigenic hormone (ghrelin) (Study 3), whereas feelings of security about such resources may conversely contribute to de-prioritization of energy-density when selecting foods (Study 4). This presentation will conclude by examining how this proposed secondary function of appetite regulation may synthesize and explain diverse phenomena such as stress-induced eating, compensatory consumption, and socioeconomic disparities in obesity.

P104 **Anxiolytic Effects Of Unhealthy Food Consumption, In Adults.**

JP PRZYBYSZ, AE CAVANAUGH, NJ MCKAY
SUNY Buffalo State, Buffalo, NY, United States

It is well established that elevated stress increases energy intake. Furthermore, when specific food items are examined, people under stress increase consumption of unhealthy food items. Although the effect that stress has on food intake has been extensively examined, why stressed individuals increase energy intake has received little attention. The current studies aimed to determine if eating unhealthy food has a suppressive effect on anxiety. The initial experiment tested whether eating an unhealthy food item decreased perceived anxiety. Participants came into the lab, rated their anxiety, and were told to eat either a Twix®, an equal weight portion of carrots, or read a magazine for five minutes. Then they rated their anxiety a second time. It was found that anxiety decreased more after eating a Twix® than eating carrots, in participants with high baseline anxiety. A limitation to this experiment was that participants were not under stress when food was consumed. Therefore, a second experiment was run that put participants through an acute laboratory stressor. In this experiment, participants came into the lab, provided baseline anxiety measurements (including perceived anxiety, salivary cortisol, and blood pressure) and underwent a laboratory stressor. After the stressor, participants provided anxiety measures a second time, and then received either a Twix®, carrots, or read a magazine. Anxiety measures were taken four more times every 10 min. Unlike the initial experiment, there was no difference in anxiety, cortisol, or blood pressure between the conditions. It was found, however, that there was a negative correlation between baseline cortisol and dietary restraint. Overall, these studies begin to provide insight into why people eat unhealthy foods during stress.

P105 **Automated Behavior Analysis Supplements Ingestive Studies**

JRB LIGHTON
Sable Systems International, North Las Vegas, NV, United States

Metabolic phenotyping systems are a mainstay of ingestive biology. They allow researchers to quantify circadian patterns and absolute amounts of energy intake and expenditure in multiple mice or rats simultaneously. Most such systems produce summarized data sets that give adequate information for many experiments. However, recording raw, synchronous system data at a high rate yields a superset of analytical tools. Chief among these is automated objective behavior recognition based on sensor interactions (e.g. feeders, water dispensers, body mass habitats, running wheels and open-field location arrays). This, in turn, supplements the basic data acquired by the system with detailed ingestive pattern analysis, time budgets, locomotion budgets, lists of behaviors with associated energy expenditures, and behavior transition probabilities that give far richer insight into the animal than simplistic summaries. Hierarchical cluster analysis based on such data can reveal otherwise invisible differences between treatments or genomes, and Markov chain analyses of transition probabilities allow rigorous, objective analysis of subtle differences in behavior without requiring video analysis. These points are explained in greater detail in the poster, and examples from recently published research are shown.

P106 **Food Intake Recruits Orosensory And Post-Ingestive Dopaminergic Circuits To Affect Eating Desire**

S EDWIN THANARAJAH[1], H BACKES[1], AG DIFELICEANTONIO[2,3], SM SMALL[2,3], JC BRUENING[1], M TITTGEMEYER[1,3]

[1]MPI for Metabolism Research, Cologne, Germany, [2]Yale University Scholl of Medicine, New Haven, CT, United States, [3]Modern Diet and Pysiology Research Center, new Haven, CT, United States

Pleasant taste as well as nutritional value guide food selection behavior. The current understanding is that orosensory features of food are secondary to its nutritional value in underlying reinforcement, but it is unclear how the brain encodes the reward value of food. Ultimately, orosensory processes and peripheral physiological signals may act on dopaminergic circuits to drive food intake. However, to what extent orosensory pathways and signals from the periphery modulate the dopamine systemis unknown.Here, we combined fMRI and PET imaging to assess systems-level activation and dopamine release in response to palatable food intake in humans. Employing a novel method to analyze time-dependent [11C]raclopride PET data, we identified immediate orosensory and, for the first time, delayed post-ingestive dopamine release. Orosensory and post-ingestive responses recruit segregated brain regions: specialized orosensory integrative pathways and higher cognitive centers. Furthermore, we identified brain areas where dopamine release reflected the subjective desire to eat and found that immediate dopamine release in these regions inhibited post-ingestive release in the dorsal striatum. Collectively, our results highlight the role of brain and periphery in interacting to reinforce food intake in humans.

P107

Gut-Brain Interaction: Exploring The Link Between Bodily States And Decision Making

AK SCHMITZ[1], M TITTGEMEYER[1,2], KE STEPHAN[3], L RIGOUX[1,3]

[1]Max Planck Institute for Metabolism Research, Cologne, Germany, [2]Modern Diet and Physiology Research Center, New Haven, CT, United States, [3]ETH and University of Zurich, Zurich, Switzerland

The prevalence of obesity is increasing at alarming rate, yet very little is known about how behavioural factors might be implicated in weight gain. Recent animal studies demonstrated at a cellular level that motivational drive is dependend on the concentration of extrasynaptic DA that is tightly regulated by hormonal signals relating to body states both in short term (nutritional status, hunger) as well as in the long run (fat reserves). This raises the question of how decision making about food intake might be connected to bodily state. In a series of experiments, we study the relationship between parameters of body composition, energy state, and cognitive traits in a group of healthy participants (N=120). In addition to a battery of questionnaires, all individuals carried out behavioral tasks to assess their impulsivity (stop signal task), incentive motivation (force task), and risk taking (fortune wheel), respectively, for monetary and food rewards. Furthermore, individuals were asked to come to the lab fasted overnight and underwent a series of anthropomorphic measurements to assess their body weight and composition. Our results show that both body composition and fasting duration have differential effects on motivation and impulsivity scores. More precisely, we find that higher body fat percentage is associated with lower motivation, irrespectively of the outcome ($p < .001$). Also, fasting increased the impulsivity for food relative to monetary outcomes ($p < .001$), an effect especially pronounced in leaner individuals ($p < .05$). Collectively, our results indicate that decision making and energy balance are more intricately coupled than previously thought and provide further impetus for studying the bidirectional relationship between body state and decision parameters.

Saturday, July 21, 2018

8:30 - 10:30 AM	Calusa ABC
Symposium 6: A Gut Feeling About Cognition	

Chair(s): Scott Kanoski

8:30 **Gut Peptides, Sex , And Food Reward**

KP SKIBICKA[1,2]

[1]Department of Physiology/Metabolic Physiology, Institute of Neuroscience and Physiology, The Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden, [2]Wallenberg Centre for molecular and translational medicine, University of Gothenburg, Gothenburg, Sweden

Neural circuitry controlling food reward has largely been investigated in male animals. This trend is perfectly mirrored by literature exploring the food reinforcement impact of gut peptides, including glucagon-like peptide (GLP-1) and ghrelin. Yet, recent data suggest that neural control of appetite and reward may differ between males and females, and therefore results obtained from male animals are not necessarily readily applicable to females. Moreover, sex steroid receptors are found in nearly all brain nuclei directly responding to gut signals, creating neuroanatomical and molecular conditions for direct interactions of these signals. Here I will explore how sex, and sex steroids alter food reinforcement effects of GLP-1, and discuss how these interactions differ as a function of neuroanatomical location. I will show both quantitative and qualitative differences between male and female responses to central GLP-1R manipulations, highlighting the importance of including both sexes in preclinical studies of food reward.

9:00 **Vagal Afferent Signaling In Gut-Brain Communication - Effects Beyond Eating**

W. LANGHANS
Physiology and Behavior Laboratory, ETH Zurich, Schwerzenbach, Switzerland

Vagal afferents are the most important neural component of the gut-brain axis. Vagal afferent signaling (VAS) plays an important role in the control of eating and metabolism. VAS supposedly also affects mood and cognition, effects often conceptualized as “gut feelings”. I will present results from a series of studies that addressed the role of VAS in emotional behaviors and cognitive functions using a rat model of subdiaphragmatic vagal deafferentation (SDA). SDA is the most selective method to disconnect all abdominal vagal afferents. In standard tests of innate anxiety (elevated plus maze, open field, and food neophobia tests), SDA rats consistently displayed reduced anxiety-like behavior compared to sham-operated control rats. On the other hand, SDA did not affect social approach behavior (two-compartment social approach test), and it increased the expression of auditory fear conditioning. These effects were associated with region-specific changes in norepinephrine and GABA levels in areas of the limbic system. In standard cognitive tests, SDA did not affect working memory in a non-spatial alternation task, nor did it influence short-, intermediate-, and long-term object recognition memory. SDA did also not affect the acquisition of positively reinforced left-right discrimination learning, but it facilitated the subsequent reversal left-right discrimination learning. This occurred without concomitant changes in motivation towards the positive reinforcer, indicating selective effects on cognitive flexibility. In summary, abdominal VAS can modulate behavioral functions beyond eating. Whereas the relative contribution of VAS to cognitive functions may be limited, it appears to be particularly relevant for innate anxiety-like behaviors.

9:30 **Microbiome Transplantation For Improvement Of Metabolic And Mental Health**

HR BERTHOUD, MB MUMPHREY, S GHOSH, JM SALBAUM, A BRUCE-KELLER
Pennington Biomedical Research Center, Louisiana State University System, Baton Rouge, LA, United States

Given their intimate interactive relationship with the mucosa, it is not surprising that gut microbiota can affect brain function and mental health via the multiple gut-brain communication pathways, and first reports using fecal microbiota transplantation (FMT) to treat neurologic diseases such as Parkinson and epilepsy have recently appeared. Mental illness and cognitive impairment are strongly associated with functional gastrointestinal disorders and with obesity, but cause and consequence is not well understood. To shed light on the specific role of gut microbiota in the neurobehavioral impairment observed in diet-induced obese mice, we used adoptive transfer of high-fat diet-shaped and control microbiota to lean

male mice and lean female mice subsequently made pregnant. We found significant behavioral impairment (increased anxiety, increased stereotypy, impaired memory) in male recipients and offspring of female recipients of obese-type (unhealthy), but not lean (healthy) microbiota in the absence of obesity. These behavioral changes were accompanied by impaired intestinal barrier function, elevated plasma endotoxin levels and impaired immune signaling and impaired synaptic and cerebrovascular integrity in brain cortical regions. Furthermore, metagenomics analysis identified a specific microbiota fingerprint potentially responsible for the neurologic impairments. To better understand the specific signaling pathways involved, we are currently studying the interaction of food, bile acids, and microbiota and their effects on mucosal gene expression and the plasma metabolome in a gut segment-specific manner. Supported by National Institutes of Health grants DK047348 (HRB) and P20-RR021945 (COBRE P&F and Phenotyping Core).

10:00 **Embodying Depression: The Interoceptive Insula And Mental Health**

K SIMMONS
Janssen Research & Development

Over the past decade a growing body of research demonstrates that the insula plays a critical role in the perception and integration in the brain of largely afferent vagal signals conveying information about the body, a faculty otherwise known as ‘interoception’. Basic cognitive neuroscience research has demonstrated that there exists a functional topography across the insula, wherein the mid-insula is particularly important for monitoring the body’s homeostatic state. As a result, it has become clear that interoception (and the mid-insula) might play a critical role in the maintenance of both physical and mental health. My talk will review recent findings from my lab demonstrating that abnormal activity in interoceptive neurocircuitry relates to the development and course of major depression disorder (MDD). For example, we have demonstrated that MDD is associated with abnormal interoceptive-related activity and functional connectivity in the mid-insula, and that this activity is predictive of depression severity. Likewise, we have demonstrated that the activity of the mid-insula may help to classify subtypes of depression, and explain why some individuals lose their appetite when the get depressed, while others eat more. Finally, at the conclusion of the talk I will integrate the findings described earlier by presenting a conceptual model based on Bayesian principles of active inference that helps to clarify the specific roles played by the mid-insula in interoceptive perception, both normatively and in illnesses like depression.

8:30 - 10:30 AM	Calusa FGH
ORAL SESSION 8: Macronutrient Effects	

Chair(s): Daniel Tome and Samantha Fortin

8:30 **(Nita Award Winner) Children Did Not Adjust Their Intake Over 5 Days In Response To Variations In Energy Density**

AD SMETHERS[1], KL KELLER[1,2], LS ROE[1], CE SANCHEZ[1], FM ZURAIKAT[1], BJ ROLLS[1]

[1]Department of Nutritional Sciences, The Pennsylvania State University, University Park, PA, United States, [2]Department of Food Science, The Pennsylvania State University, University Park, PA, United States

Evidence is needed to examine the proposition that young children regulate their intake in response to energy surfeits or deficits. Therefore, we tested whether preschool children adjusted their intake in response to changes in dietary energy density (ED) over a 5-day period. In a crossover design, we provided all meals and snacks during three 5-day periods to 49 children aged 3-5 y in their childcare centers. In each 5-day period, 3 main dishes and 1 snack per day were served with systematic variations in ED: baseline ED, ED increased by 20%, or ED decreased by 20%. Foods and milk were consumed *ad libitum* and weighed intakes were determined. Compared to baseline, serving higher-ED main dishes and a snack increased daily energy intake by 9% (83±16 kcal) and serving those lower in ED decreased intake by 8% (74±16 kcal; both $p< 0.0001$). Varying ED led to sustained changes in children's energy intake, as the slopes of energy intake over the 5 days did not converge ($p=0.20$). Changes in energy intake resulted from children eating a similar weight of the main dishes and the snack in both the higher-ED and lower-ED conditions as they did at baseline ($p>0.23$). Furthermore, children did not adjust intake of unvaried snacks ($p=0.37$) or vegetable side dishes ($p=0.78$) compared to baseline. Thus, in response to energy surfeits or deficits from the changes in main dish and snack ED, children did not preferentially eat more or less of unvaried foods in order to regulate energy intake. Changes in ED over 5 days led to sustained effects on children's energy intake. These results challenge the premise that young children adjust their intake in response to either positive or negative energy imbalances. Funding: DK082589, USDA Grant 2011-67001-30117

8:45 **Consuming Sucralose Together With Maltodextrin Rapidly Decreases Brain And Insulin Sensitivity To Sugar**

JR DALENBERG, BP PATEL, MG VELDHUIZEN, Y NAKAMURA, PC VINKE, DM SMALL
Yale University School of Medicine, New Haven, CT, United States

Much controversy surrounds the potential impact of non-nutritive sweeteners (NNSs) on health. Positive, negative and negligible effects have all been reported. One influential theory that relates NNS consumption to negative health outcomes is the uncoupling hypothesis proposed by Swithers and Davidson. This hypothesis posits that uncoupling sweetness from energy impairs the ability of sweet taste to regulate behavioral and metabolic responses to sugars thus leading to the development of obesity and glucose intolerance. Here we sought to test this hypothesis in healthy humans. Metabolic (OGGT), neural (fMRI), and sensory measures (intensity and sweet taste preference ratings) were collected from 39 adults before and after consuming novel beverages over a period of two weeks. Participants were randomly assigned to drink equally sweet beverages sweetened with sucralose, 120 Kcal sucrose, or sucralose plus 120 Kcal maltodextrin (SUMA). We predicted that if the uncoupling hypothesis is true then participants in the sucralose, but not the sucrose or SUMA groups should show reductions in glucose tolerance, and perceptual and neural response to sweet but not salty, sour or bitter tastes.
Contrary to our prediction, we found significantly decreased insulin sensitivity in the SUMA group. The change in insulin sensitivity within this group negatively correlated with brain response to sweet, but not other tastes, in dopamine source and target areas. No changes in perception were observed. These results demonstrate that consumption of sucralose together with maltodextrin rapidly decreases brain and metabolic responsiveness to sugar. Future research should address whether our findings generalize to other NNSs and carbohydrates and whether these effects are reversible.

9:00 **Long-Term Effects Of Increased Protein Intake During Weight Maintenance After Weight Loss On Intrahepatic Lipid Content And Implications For Insulin Sensitivity - A Preview Study**

M DRUMMEN[1,3], E DORENBOS[2,3], ACE VREUGDENHIL[2,3], A RABEN[4], M FOGELHOLM[5], MS WESTERTERP-PLANTENGA[3], TC ADAM[1,3]

[1]Department of Nutrition and Movement Sciences, Maastricht University Medical Centre +, Maastricht, Netherlands, [2]Centre for Overweight Adolescent and Children's Health Care (COACH), Department of Paediatrics, Maastricht University Medical Centre +, Maastricht, Netherlands, [3]NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Centre +, Maastricht, Netherlands, [4]Department of Nutrition, Exercise and Sports, University of Copenhagen, Copenhagen, Denmark, [5]Department of Food and Nutrition Sciences, University of Helsinki, Helsinki, Finland

The PREVIEW study (EU-FP7-nr. 312057) aims to identify most effective lifestyle components in the prevention of T2D. The present sub-study assessed the effects of weight loss and subsequent weight maintenance comprising two diets differing in protein intake on intrahepatic lipids (IHL) and implications for insulin sensitivity. A subgroup of 25 PREVIEW participants, (BMI: 31.5±3.7kg/m^2; IHL: 9.3±8.4%; HOMA-IR: 3.8±1.6; Matsuda insulin sensitivity index (ISI): 3.3±2.7) started an 8-week low energy diet, followed by a 2-year weight maintenance period with either high protein (HP) or medium protein (MP) dietary guidelines. At baseline, after 6 months and after 2 years, IHL was determined by magnetic resonance spectroscopy. Glucose and insulin concentrations were determined during an oral glucose challenge to assess HOMA-IR and ISI. Protein intake was measured with 24-h urinary nitrogen excretion. In this subgroup, the difference in daily protein intake (g/kg, MP: baseline: 0.81±0.2; 6 months: 1.03±0. 2; 2 years: 1.10±0.5, HP: baseline: 0.86±0.2; 6 months: 1.12±0.3; 2 years: 0.95±0.3) did not reach statistical significance, and BMI and IHL did not change differently during the intervention. In the whole group, BMI, IHL, HOMA-IR and ISI were favourably changed at 6 months and 2 years compared to baseline ($p< 0.05$). Mixed model analysis showed that independent of BMI, protein intake (g/d) at 6 months was inversely related to IHL ($r=-0.03$; $p< 0.05$). Overall, IHL was positively related to HOMA-IR ($r=0.10$; $p< 0.01$) and inversely related to ISI ($r= -0.17$; $p< 0.01$), independent of BMI. In conclusion, a 2 year medium- to high-protein energy restricted diet reduced IHL. Independently of BMI changes, IHL was inversely related to insulin sensitivity.

9:15 **Type Of Dietary Fat Affects Dopamine Terminal Function: Saturated Vs. Unsaturated**

C WALLACE, CN BARNES, BS JACOBOWITZ, SC FORDAHL
UNC-Greensboro, Greensboro, NC, United States

Saturated fat (SF) intake is linked to disrupted dopamine neurotransmission, including attenuated dopamine transporter (DAT) function and reduced dopamine receptor D_2 binding. Reduced DAT function degrades tight control of synaptic dopamine, which is thought to contribute to palatable food intake; whereas reduced D_2 binding availability may disrupt the D_2-mediated nucleus accumbens (NAc) to hypothalamic satiety circuit. Recent reports show saturated fat enhances the behavioral effects of dopamine agonists, but unsaturated fatty acids do not, thus we sought to examine whether unsaturated fat intake altered dopamine release and uptake kinetics at dopamine terminals. C57BL/6 mice were fed low-fat food, or iso-caloric high-fat food containing identical amounts of either SF, unsaturated fat in the form of omega-3 and omega-6-rich flax seed oil (FSO), or an equal blend of saturated fat and FSO (BLEND). All high-fat groups consumed a similar amount of kcals per day, but the FSO group gained significantly less body weight than the SF and BLEND groups, and displayed similar fasting blood glucose and glucose clearance as low-fat controls. Using *ex-vivo* voltammetry, no differences in NAc dopamine release or D_2 auto-receptor sensitivity were observed across groups, but dopamine uptake was significantly attenuated in SF compared to low-fat, FSO, or BLEND groups. Interestingly, body weight predicted uptake deficits in the SF group. These data suggest that mono- and poly- unsaturated fats do not engender the same metabolic and neurochemical deficits as SF.

9:30 **Interacting Effects Of Fat And Sugar Consumption On Opioid And Dopamine Receptors In The Nucleus Accumbens**

LL KOEKKOEK[1,2], L EGGELS[1,2,3], UA UNMEHOPA[1], K LAMUADNI[1], JD MUL[1,2], MJ SERLIE[1], SE LA FLEUR[1,2]
[1]Department of Endocrinology and Metabolism, Academic Medical Centre, Amsterdam, Netherlands, [2]Metabolism and Reward Group, Royal Academy of Arts and Sciences, Netherlands Institute for Neuroscience, Amsterdam , Netherlands, [3]Laboratory of Endocrinology, Department of Clinical Chemistry, Academic Medical Centre, Amsterdam, Netherlands

High-caloric diets, rich in fat and sugar, are dominant drivers of the current obesity epidemic. A free choice high-fat high-sugar (fcHFHS) diet, a multi-component choice diet model that mimics human consumption of high-caloric diets, is associated with long-lasting hyperphagia, increased body weight and changes in arcuate neuropeptide expression. We have recently proposed a mechanistic model, which includes alterations in μ-opioid and dopamine receptor function in the nucleus accumbens (NAc), that can explain how simultaneous access to both fat and sugar induces persistent hyperphagia. To further test this model, rats received a regular chow diet (RCD) or a free choice high-fat (fcHF) diet, and were allowed to drink a 30% sugar solution for 5 minutes per day. This allowed us to determine the direct effects of sugar drinking on NAc gene expression, and if this is altered by the consumption of a fcHF diet. In a large cohort of rats (n=66), sugar drinking decreased μ-opioid receptor gene expression in the NAc in RCD animals compared to controls, whereas it increased μ-opioid receptor gene expression in fcHF animals (interaction effect fcHF diet*sugar: $p=0.0022$). Similar responses were observed for the dopamine receptor D2 (DRD2; interaction effect fcHF diet*sugar: $p=0.0133$). No changes were observed for δ-opioid or κ-opioid receptor gene expression. Our findings add to the evidence that concurrent fat and sugar consumption interacts on μ-opioid- and DRD2 function in the NAc, suggesting that these receptors could mediate the interacting effects fat and sugar consumption on brain-driven metabolic behavior.

9:45 **Effects Of A Free Choice High-Fat, High-Sugar Diet On Pancreatic Insulin And Vasoactive Intestinal Polypeptide Immunoreactivity In Male Wistar Rats**

C DIEPENBROEK[1,3], UA UNMEHOPA[1], Z CASTRICUM[1], L EGGELS[1,2,3], MJ SERLIE[1], SE LA FLEUR[1,3]

[1]Department of Endocrinology and Metabolism, Academic Medical Center, University of Amsterdam , Amsterdam , Netherlands, [2]Laboratory of Endocrinology, Department of Clinical Chemistry, Academic Medical Center, University of Amsterdam, Amsterdam , Netherlands, [3]Metabolism and Reward group, Netherlands Institute for Neuroscience, an Institute of the Royal Netherlands Academy of Arts and Sciences, Amsterdam, the Netherlands, Amsterdam , Netherlands

Increased vagal activity has been associated with obesity and concomitant hyperinsulinemia. Parasympathetic-pancreatic nerve endings release, among others, the neuropeptide vasoactive intestinal polypeptide (VIP), which stimulates the early phase glucose-induced insulin secretion. Whether dietary components, that induce obesity, affect VIP β-cell innervation and thereby the glucose-induced insulin response, is currently unclear. We have previously shown that rats on a free-choice, high- fat, high-sugar (fcHFHS) diet show obesity, hyperphagia, and glucose intolerance, with an impaired insulin response. We here investigated whether the blunted glucose-induced insulin response is associated with altered VIP innervation of the of pancreatic β-cells and/or by altered insulin content. Male rats received a fcHFHS or chow diet for 4 weeks, after which pancreases were dissected, fixated in paraformaldehyde (4%), and embedded in paraffin. Pancreatic sections of chow (n=6) and fcHFHS-fed rats (n=4) were cut and immunostained for insulin, and VIP, and immunoreactive areas (in nine sections per rat) were quantified as a measure of insulin content and VIP innervation density respectively. Rats consuming a fcHFHS diet for 4 weeks showed no difference in pancreatic insulin immunoreactivity (10.69±0.53 vs 10.76±0.73, p=0.93). Interestingly, total VIP area (0.24±0.03 vs 0.12±0.02, p=0.02) and VIP immunostaining per islet structure was decreased in fcHFHS-fed rats compared to chow-fed rats (10.4±1.78 vs 4.67±0.90; p=0.04). Together, these results may point towards a change in parasympathetic innervation of the β-cell after 4 weeks of fcHFHS diet consumption, which may explain the impaired glucose-induced insulin response.

10:00 **Potato Resistant Starch Supplementation Improves Microbiota Dysbiosis, Inflammation And Vagal Signaling In High Fat Fed Rats**

EA KLINGBEIL, CR CAWTHON, RA KIRKLAND, CB DE LA SERRE
University of Georgia, Athens, GA, United States

Chronic high fat (HF) feeding leads to gut microbiota dysbiosis associated with translocation of pro-inflammatory bacterial products to the circulation. Subsequent low grade inflammation is sufficient to alter vagally-mediated satiety and induce hyperphagia, and weight gain. Promoting bacterial fermentation and short chain fatty acids (SCFAs) production has been shown to enhance gut integrity and improve systemic inflammation. Resistant starch (RS) digestion in the small intestine is limited, can reach the distal intestine and be fermented by bacteria. We hypothesized that potato RS supplementation in HF fed rats would lead to compositional changes in gut microbiota composition associated with improved vagal signaling. Wistar rats (n=8/group) were fed a low fat chow (LF, 13% fat), HF (45% fat) or HF supplemented with 12% potato RS (HFRS, isocaloric to HF) diet. Rats were evaluated for response to gut-originating satiety peptide cholecystokinin (CCK, 2μg/kg), oral glucose tolerance, and after 8 weeks on respective diets brainstem, cecal, and fecal contents were collected. Vagal innervation was assessed in brainstem sections by staining for c fibers using isolectin b4 (IB4). RS supplementation led to beneficial microbiota changes. HFRS fed rats ate significantly less than HF fed rats (2389±218 vs. 2635±293 kcal). Glucose tolerance was significantly improved in HFRS rats at 90 and 120 minutes post-oral gavage. CCK-induced reduction in food intake (-1.7±1g in LF rats) was abolished in HF fed rats and restored in HFRS rats (-1.3±0.9g). Brainstem IB4 staining was significantly decreased in HF fed but not HFRS rats. Microbiota manipulation via PRS dietary supplementation prevented HF diet-induced vagal remodeling, loss in CCK-induced satiety and hyperphagia.

10:15 **Fats And Sugars Have Opposing Effects On Vagal Mediated Food Intake**

M MCDOUGLE, W HAN, I DE ARAUJO, G DE LARTIGUE
JB Pierce/Yale, New Haven, CT, United States

Vagal afferent neurons (VAN) provide information about meals to inhibit food intake (FI). The role of VAN in mediating the effects of different macronutrients remains unclear. **Method**: A retrograde virus expressing Cre-recombinase (CAV2-hSyn-Cre-GFP) was injected into the stomach and duodenum walls to drive Cre in peripheral gut-innervating VAN (n=5). The Cre-inducible Gs-coupled designer receptor (AAV5-Ef1a-DIO-rM3Ds-tdTomato) was bilaterally injected in nodose ganglia of the same mice. The number and timing of individual licks for intralipid (0.5kcal/ml and 3.0kCal/ml) or sucrose (0.5kCal were quantified over 3 hours in food restricted mice receiving either CNO (IP; 5mg/kg) or vehicle (100ul). **Results:** In mice licking for lipids, increasing GI-VAN excitability with CNO rapidly reduced lick number by >50% compared to vehicle ($p < 0.001$), irrespective of the caloric concentration. In mice licking for sucrose, CNO slowly increased lick number by 40% compared to vehicle ($p < 0.01$). CNO had no effect on intake in sham controls (n=5; $p>0.05$). **Conclusion:** Vagal feeding control is dependent on macronutrient signaling.

10:30 - 11:00 AM	Calusa DE
Coffee Break	

11:00 - 12:00 PM	Calusa ABC
MARS LECTURE 4	

Chair(s): Guillaume de Lartigue

11:00 **The Dorito Effect**
M SCHATZKER
Chair of the Social Change Advisory Committee for the Modern Diet and Physiology Research Center

12:00 - 2:30 PM	Lunch On Own
Lunch on Own	

2:30 - 4:15 PM	Calusa ABC
AWARDS SESSION	

Chair(s): Bob Ritter, Kellie Tamashiro, Larry Reagan and Stephen Woods

2:30 **Introduction**

2:45 **Hoebel Prize For Creativity**
A GELIEBTER
Columbia University

3:15 **Alan N. Epstein Research Award**
E KRAUSE
University of Florida

3:45 **Distinguished Career Award**
W LANGHANS
ETH Zurich

4:15 - 5:15 PM	Calusa ABC
Business Meeting	

7:00 - 12:00 AM	Estero Ballroom
BANQUET	