



31st Annual Meeting of the Society for the Study of Ingestive Behavior

Printable Program and Abstracts

July 9-13, 2024
Chicago, IL

Tuesday, July 9, 2024

12:00 - 3:00 PM	Illinois Boardroom
SSIB BOARD MEETING (INVITATION ONLY)	

1:00 - 6:30 PM	Sheraton Promenade West
Registration	

4:45 - 6:00 PM	Ballroom I-II
Opening Greetings & MARS Lecture 1	

Chair(s): Gina Leininger

4:45 **Opening Greetings**
Scott Kanoski

5:00 **Functional Organization Of Feeding-Related Signals In The Lateral Parabrachial Nucleus**
Rachel A Essner^{1,2}, Kiersten Ruda¹, Hannah J Choh¹, Oren Amsalem¹, Hakan Kucukdereli¹, Mark L Andermann^{1,2,3}
¹Division of Endocrinology, Beth Israel Deaconess Medical Center, Boston, MA, United States, ²Program in Neuroscience, Harvard University, Boston, MA, United States, ³Department of Neurobiology, Boston, MA, United States

During consumption, food activates mechano- and chemosensory afferents as it moves from the mouth through the esophagus, stomach, and small intestine. However, the real-time dynamics with which neurons in downstream satiety-promoting neurons in the brainstem become active during natural consumption remains unknown. We used X-ray fluoroscopy to track the real-time movement of liquid food (Ensure) through the upper gastrointestinal (GI) tract during feeding. We then related food transit dynamics to the feeding-related activity of single neurons in the brainstem lateral parabrachial nucleus (LPBN), which integrates multimodal bodily signals, responds to input from the GI tract, and suppresses appetite. We developed a novel approach for chronic, 3D imaging of LPBN via a GRIN lens implanted above the surface of LPBN. We found that liquid food enters the stomach 3 s after the onset of consumption, and that a subset of LPBN neurons become active on this same timescale (Late cells), suggesting that these Late cells are sensitive to stomach signals. In support of this hypothesis, we also found that Late cells strongly respond to stomach distension and to other stimuli that activate stomach-innervating afferents, including the satiety hormone cholecystokinin and the nausea-inducing agent LiCl. Other LPBN neurons have a transient or sustained response at the onset of consumption (Early cells), suggesting that they respond to licking and/or food transit through the mouth and esophagus. Finally, Early and Late cells were spatially segregated, indicating functional topography of GI tract sensitivity. Together, our results reveal distinct populations of LPBN neurons that respond to regional stimuli from the GI tract during food intake.

6:00 - 8:00 PM	Riverwalk A
Opening Reception & Exhibits	

Wednesday, July 10, 2024

8:00 - 6:00 PM	Sheraton Promenade West
Registration	
8:30 - 10:15 AM	Riverwalk A
Poster Session 1 & Exhibits	

- P100 **Testing The Impact Of Negative And Positive Mood States On Motivation To Eat In Women With Binge Eating**
Lindsay Bodell, Kendall Schmidt, Taylor Breddy
Western University, London, ON, Canada

Introduction. Although evidence suggests that negative affect impacts the likelihood of binge eating episodes, little is known about why this association exists. One possibility is that negative affect increases the reward value of food, particularly in individuals with binge eating. This pilot study used a between-subjects experimental design to examine the influence of negative, positive, or neutral mood states on the reward value of food (e.g., motivation to eat) in women with or without binge eating. **Methods.** Participants were 84 women with (N=53) or without (N=31) binge eating. Participants were randomly assigned to complete a standardized mood induction procedure in which they wrote about a sad, happy, or neutral autobiographical event. After the mood induction, participants completed a computerized progressive ratio task designed to measure motivation to eat. **Results.** Consistent with prior studies, women with binge eating demonstrated greater motivation to eat on the reward task compared to women without binge eating, with a small-medium effect size (Cohen's $d = 0.45$). However, contrary to hypotheses, the negative mood condition was associated with lower motivation to eat than the positive or neutral condition, regardless of binge eating status. **Conclusions.** Data suggest that reward value of food may differ in individuals with and without binge eating, regardless of one's current mood state. Given the preliminary nature of these findings, more participants are needed to determine the stability of these effects.

- P101 **The Effect Of Sucking Measurement Across Devices On Infant Milk Intake**
Amanda K Crandall¹, Ashley N Gearhardt², Alison L Miller³, Cin Cin Tan⁴, Julie C Lumeng¹
¹University of Michigan, Medical School, Department of Pediatrics, Ann Arbor, MI, United States, ²University of Michigan, College of Literature, Science, and the Arts, Department of Psychology, Ann Arbor, MI, United States, ³University of Michigan, School of Public Health, Department of Health Behavior & Health Education, Ann Arbor, MI, United States, ⁴University of Toledo, College of Arts and Letters, Department of Psychology, Toledo, OH, United States

Infant sucking behavior can be objectively measured in clinical or research contexts using devices that connect to infant bottles. Little is known about how such devices may impact behavior during a feeding interaction. This analysis sought to explore, among 4-month-old infants, how the presence of a sucking measurement device and the type of device may impact milk intake, feeding duration, clarity of infant cues, and maternal sensitivity to infant cues and distress. The current study included 130 healthy full-term infants (51% male) offered a bottle fitted with the Nfant Feeding Solution, the NeoNur, or no device by their caregivers. This difference in sucking measurement was due to a protocol change and was not part of the original study design. The feeding interactions were timed, and the bottles were weighed pre- and post to calculate feeding duration and milk intake. The Parent-Child Interaction Feeding and Teaching Scales (NCAST) questionnaire was coded on observable behaviors to describe the quality of a naturalistic feeding interaction. Multiple regression models controlling for exact age, bottle feeding intensity, time since the last feeding, and the amount consumed at the last feeding were calculated to assess the hypotheses. Total milk intake was reduced by 17.14 grams among infants who received the Nfant bottle compared with no measurement device ($p = 0.045$). Conversely, feeding duration increased by 4.12 minutes among those who received the NeoNur compared with no device ($p = .034$). There were no differences between the device groups regarding the clarity of infant cues or maternal sensitivity to infant cues or distress. The presence of the sucking measurement devices changed infant feeding behavior but not the quality of the feeding interaction.

- P102 **Characterizing The Role Of Mu Opioid Receptors In Metabolism And Behavior**
Diego De Gregorio, Daniel C. Castro
Biophotonics Research Center, Mallinckrodt Institute of Radiology, Washington University School of Medicine in Saint Louis, 63110, Saint Louis, MO, United States

Since the 1970s, opioids have shown significant but variable effects on metabolism across different species. One consistent finding is their impact on enhancing glucose metabolism and insulin secretion, hinting at interactions with the endocrine pancreas. Here, we aim to understand how endogenous MOPRs regulate pancreas function through genetic and pharmacological interventions. To assess the influence of MOPR loss on ingestive behaviors, we measured 24-hour ad libitum food consumption using Feeding Experimental Devices (FEDs) in C57BL/6J wildtype and OPRM1 knockout (MOPR-deficient) mice. Male MOPR knockout (KO) mice (n=15) exhibited significantly increased body weight and food intake compared to wildtype controls (n=15) ($F=19.99$, $p=0.0001$, $t=5.765$; $F=10.60$, $p=0.0009$, $t=3.756$). However, no significant differences were observed in feeding frequency and bout sizes. Female MOPR KO mice (n=14) showed no differences compared to controls (n=15). Glucose tolerance tests (GTT) and insulin tolerance tests (ITT) in KO (n=10) and wildtype mice (n=10) showed enhanced glucose tolerance at 30 and 60 minutes in both sexes at a young age (10-12 weeks) ($F=15.78$, $p=0.0023$ and $p=0.0014$; $t=3.957$ and $t=4.118$, respectively). However, this effect was absent at a later age (25-27

- weeks). Pharmacological antagonism of MOPRs in wildtype mice significantly impaired glucose tolerance in males (n=4) but not females (n=3). Future plans include assessing age-related changes in GTT and ITT and further pharmacological experiments with DAMGO and naloxone (Narcan).
- P103 Self-Selected Diets: Exploring The Factors Driving Food Choices And Satisfaction With Dietary Variety**
 Lauren E Ehrmantraut¹, Joseph P Redden², Traci Mann³, Nathaniel E Helwig⁴, Zata M Vickers¹
¹Department of Food Science and Nutrition, University of Minnesota, Saint Paul, MN, United States, ²Marketing Department - Carlson School of Management, University of Minnesota, Minneapolis, MN, United States, ³Department of Psychology, University of Minnesota, Minneapolis, MN, United States, ⁴School of Statistics, University of Minnesota, Minneapolis, MN, United States
- Food choices determine the nutrients and other substances that build and maintain our bodies as well as consumer demand for food products. People choose specific foods, and those choices are strongly influenced by many factors. Our goal was to examine the reasons participants gave for choosing each of the foods they consumed during a 4-week study, how those influencers differed for different food classes, and whether the influencers predicted satisfaction with their dietary variety. Participants maintained a 28-day online food diary. Each week, they rated their satisfaction with the variety in their diets and the impact of 13 choice influencers on each of the foods they consumed. We recorded the frequency at which each choice influencer was rated as having high, moderate, low, or no impact on selection. We grouped each food into one of 17 food classes to weigh the importance of each influencers for consuming each of these food classes. *Liking*, *hunger*, and *convenience* were most frequently selected as having a high impact on food choice. The *presence on a menu*, *only thing served*, and *special occasion* were most frequently selected as having no impact on food choice. Liking was generally the highest rated choice influencer across food classes. Liking had high to moderate impact on the consumption of healthier food classes such as the fruits and vegetable classes at similar proportions as less healthy food classes such as the alcohol and desserts classes. Satisfaction with weekly variety was best predicted by *liking*; *convenience* generally reduced satisfaction.
- P104 Leptin Resistance Predicts Positive Energy Balance But Not Appetitive Traits In 4-10-Year-Old Children: A Secondary Analysis Of Observational Data**
 Amelia E Fouts, Alysha B Everett, Paula C Chandler-Laney
 University of Alabama at Birmingham, Birmingham, AL, United States
- Leptin is an adipokine that binds to hypothalamic receptors to regulate satiety. Leptin resistance is associated with greater adiposity in children; however, its association with appetitive traits and energy balance is less understood. The objectives of this study were to (1) test the hypotheses that leptin resistance is associated with greater food responsiveness, less satiety, and positive energy balance, and (2) investigate whether any such association is moderated by child weight status. Leptin resistance was calculated as fasting leptin concentration over fat mass index. Food responsiveness and satiety were assessed with the Child Eating Behavior Questionnaire. Energy balance was calculated as total energy intake minus resting and activity-related energy expenditure. Weight status was defined as body mass index (BMI) <85th or ≥85th percentile. Regression models evaluated the association of leptin resistance with outcomes of interest and tested the interactive effect of weight status and leptin resistance. In children 4-10 years old (n=81), leptin resistance was not associated with food responsiveness (b<0.01, SE=0.31; p=0.99) or satiety (b=-0.16, SE=0.17; p=0.36). Leptin resistance was associated with energy balance independent of race, sex and Tanner stage (b=3314.90, SE=1030.01; p<0.01). There was an interaction of weight status and leptin resistance such that leptin resistance predicted positive energy balance for children with a BMI <85th percentile (b=1589.41, SE=463.68; p<0.01), but not for children with a BMI ≥85th percentile. Results suggest that among children without overweight, leptin resistance is associated with over-consumption relative to energy needs, but this association is absent for children with overweight/obesity.
- P105 Examining Genetic Sensitivity To Bitterness In The Context Of Two Food Preference Learning Interventions For Preschoolers**
 Vaishali Gupta¹, Sara Tauriello¹, Stephanie Anzman-Frasca^{1,2}
¹Department of Pediatrics, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY, United States, ²Center for Ingestive Behavior Research, University at Buffalo, Buffalo, NY, United States
- Genetic differences in sensitivity to bitter tastes may contribute to children's rejection of vegetables. Food preference learning interventions, such as repeated exposure (RE) and associative conditioning (AC), can increase vegetable acceptance, yet few studies have examined how bitterness sensitivity may moderate outcomes. We explored the role of genetic sensitivity to bitterness in two food preference learning interventions for preschoolers. Fifty parents with 3-to-5-year-old children were recruited for a 3-week intervention and randomized to receive 9 repeated exposures (RE) to an initially non-preferred target vegetable or 9 exposures paired with parent-child activities (AC). Child acceptance of 7 vegetables (4 bitter) was collected at pre- and post-test. Bitterness sensitivity was assessed at post-test with paper 6-n-propylthiouracil strips (n=42 children; 52% female; 21% Black; 55% white; 36% bitter-sensitive, or "tasters"). We used chi-square, sign, and ANOVA tests to examine whether acceptance of bitter vegetables at baseline ("yummy" or "just OK" vs. "yucky" or "would not taste") differed by taster status and whether taster status moderated intervention effects on target vegetable acceptance. Tasters were less likely than non-tasters to accept 3 of the 4 bitter vegetables at baseline (broccoli: $X^2=2.8$, p=.09; cauliflower: $X^2=3.9$, p=.07; Brussels sprouts $X^2=5.1$, p=.02). Target vegetable acceptance increased from pre- to post-test overall (p<.05), with no interaction between study group and bitterness sensitivity or main effect of bitterness sensitivity predicting acceptance at post-test. Findings support the potential of both of these intervention approaches to promote vegetable acceptance among tasters who may have lower initial acceptance of bitter vegetables.
- P106 Exogenous Lubrication And Failure To Compensate May Facilitate Energy Overconsumption From Salty Snacks Served With Dip**
 Madeline M Harper^{1,2}, Paige M Cunningham^{1,2}, John E Hayes^{1,2}

Faster eating promotes energy intake. Exogenous lubrication from dips facilitates oral processing and may increase eating rate and/or food intake. In two randomized crossover studies, we investigated how increasing lubrication through the addition of dips influenced ad libitum snack intake. Study 1 (46 adults) compared intake of ranch-flavored tortilla chips with or without energy-matched ranch dip. Total energy intake was 77% greater with dip, but there was no difference in chip intake (i.e., no reduction in chip intake to compensate for additional dip intake). The dip condition yielded a faster total eating rate, but there was no difference in chip eating rate between conditions. Study 2 (47 adults) compared intake for pretzels served alone (control) to pretzels served with a matched-energy density hummus (added oil) or reduced-energy density hummus (added water). Total energy intake was greater in the dip conditions (control

P107

Unlimited Food Availability Induces Overeating And Weight Gain In Mice

Alexxai Kravitz, Mason Barrett

Washington University in Saint Louis, Saint Louis, MO, United States

Obesity is a major risk factor for multiple chronic illnesses, including diabetes, cardiovascular disease, and psychiatric disorders. While there are many causes of obesity, the primary drivers of obesity in recent decades are changes in the nutritional content of modern diets, and the proliferation of low-cost calorie dense food. While prior studies have demonstrated that increasing the fat content and caloric density of food drives overeating and obesity in mice, fewer studies have tested how increasing the cost of obtaining high-fat food may control overeating and weight gain. Here, we hypothesized that increasing the cost of high-fat food would limit both over-eating and weight gain in mice. To test this hypothesis, we designed a device that dispensed high-fat diet to mice either freely (free access) or after mice completed one nose-poke to access high-fat diet for sixty seconds (nose-poke access). This device fits in the home-cage with mice and was their only source of food throughout the experiments. Mice in both the free access and nose-poke access tests were allowed to access the device around the clock and interact with it as much as they wanted. In our first experiment, we exposed mice (n=6) to alternating five-day phases of free access or nose-poke access for high-fat diet. On average, mice gained 0.64g during the free access phase and lost 0.12g during the nose-poke access phase (two-tailed paired t-test, $p < 0.005$), supporting our hypothesis that increasing the cost of high-fat diet, even by as little as one nose-poke, reduced weight gain in mice. In a second experiment, we maintained two new groups of mice on either free-access (n=7) or nose-poke access (n=7) high-fat diet for six weeks. The free-access group consumed 16% more high-fat diet than the nose-poke access group (two-tailed independent t-test, $p = 0.038$), and gained 2.7g per week, compared with only 1.3g per week in the nose-poke access group (two-tailed independent t-test, $p = 0.003$). We conclude that the free availability of calorie dense food promotes overeating, and that imposing a small cost (one nose-poke) reduces high-fat diet intake and weight gain in mice. Our research highlights the importance of environmental modifications as a component of weight management strategies to combat obesity.

P108

Apolipoprotein A4 Elevates Energy Expenditure In Hfd-Fed Mice.

Zachary LaRussa¹, Hsuan-Chih Kuo¹, Mengyang Xu², Haifei Shi², Chunmin Lo¹

¹Ohio University, Athens, OH, United States, ²Miami University, Oxford, OH, United States

Obesity results from the imbalance of energy intake and energy expenditure. Apolipoprotein A4 (ApoA4) is a well-known satiation protein produced by the small intestine in the presence of dietary lipids. However, chronic consumption of high-fat diets (HFD) attenuates the production of intestinal ApoA4 normally seen in the response to dietary lipids. The hypothesis of the current study was that increased levels of plasma ApoA4 would enhance energy expenditure and subsequently attenuate HFD-induced obesity. Food intake, body weight, body composition, energy expenditure and locomotor activity were determined in HFD-fed mice with APOA4 mini-pump infusion. Relative to their controls, HFD-fed mice with increased levels of APOA4 had reduced body weight gain, fat mass, and levels of plasma lipids and leptin, but enhanced energy expenditure, despite not altering food intake and locomotor activity. In conclusion, maintenance of elevated levels of plasma APOA4 appears to correlate with elevation of energy expenditure and subsequent protection against HFD-induced obesity in mice.

P109

Investigation Of The Relationship Between Sweet Taste Liking Profiling And Bmi

James Makame, Alissa Nolden

University of Massachusetts, Amherst, Amherst, MA, United States

The food-health nexus has increasingly become a focal study area for sensory-consumer researchers, with a growing awareness of the role chemosensation can have on dietary choices, health, and well-being. Sweet taste perception has traditionally been an important taste sensation due to the link between sugar intake and body mass index (BMI). This study aims to explore individual differences in consumers' liking and taste perceptions, using the sweet liker status (SLS) which may further relate to diet-related non-communicable diseases. Sensory and hedonic data (sucrose aqueous solutions: 5 levels) was collected from 121 consumers using a generalized Labelled Magnitude Scale and generalized bipolar hedonic scale, respectively. Agglomerative Hierarchical Clustering produced 3 stable clusters. The overall BMI was 24.8 ± 5.0 . SLS clusters and BMI, taste perception, liking, and food intake variables relationships were tested using ANOVA ($p \leq 0.05$), external preference mapping (EPM), regression analysis, and Principal Component Analysis (PCA). As expected, taste intensity perception and liking differed significantly by SLS cluster, and SLS phenotyping was aligned with BMI based on multivariate PCA. The high sweet liker cluster correlated positively with higher BMI. In contrast, BMI was negatively correlated with the sweet sensitive low sweet liker cluster. However, ANOVA revealed that BMI was not significantly different across clusters. Sweet taste phenotyping and external preference mapping can be used to infer correlations between perceptions of sweetness and BMI, with further research needed to determine if sweet taste perception is useful tool to identify individuals who are at risk of obesity, for targeted public health intentions.

P110

Subjective Responses To Alcohol Consumption In Women With A History Of Metabolic Surgery: Does Alcohol Feel Like A Different Drug?

Mariel Molina-Castro¹, Blair Rowitz^{2,3}, M. Yanina Pepino^{1,2,3}

Metabolic surgery is highly effective in treating obesity; however, there is a concern about the development of alcohol misuse after roux-n-Y gastric bypass (RYGB) and sleeve gastrectomy (SG). Understanding the mechanism underlying this association is of clinical relevance and the aim of the current study. Of note, drinking alcohol after these surgeries results in blood alcohol concentrations that resemble those obtained after administering alcohol intravenously. Here, we determined whether the surgery-related changes in alcohol pharmacokinetics result in the perception of alcohol effects as if it was a different drug associated with more liking/wanting. Using a cross-sectional study design, we evaluated women who underwent RYGB/SG 1 to 5 years ago (n=15) and non-operated control women (n=14) of similar age, BMI, and alcohol consumption patterns. Women were assessed over two visits: in randomized order, they consumed an alcohol drink or a non-alcohol placebo drink. Before and after drinking, they completed the Drug Effects Questionnaire, the Biphasic Alcohol Effects Scale (BAES, to measure alcohol-induced stimulation and sedation); and the Addiction Research Center Inventory (to assess effects associated with several psychoactive drugs). We found that on the alcohol day, women post-surgery felt more of the “high” and wanted more alcohol than the control group. Interestingly, BAES scores were similar between groups, but the post-surgery group felt more LSD-like effects and drunkenness after consuming the alcoholic drink than the control group. Overall, alcohol was not a different drug, but subjective effects were intensified. These changes in alcohol's subjective effects may contribute to the observed increase in the risk for alcohol misuse after RYGB and SG.

P111 **Associations Between Parent Feeding Practices And Child Appetitive Traits In Children With Overweight And Obesity.**

Mieko P. Pretlow, Ellen K. Pasquale, David R. Strong, Kyung E. Rhee, Dawn M. Eichen, Lauren N. Hamel, Kerri N. Boutelle
University of California San Diego, La Jolla, CA, United States

Parents play a significant role in shaping their children's eating behaviors via feeding practices. While evidence exists supporting associations between parent feeding practices and child appetitive traits from infancy to early childhood, very little information is available on these relationships among school-aged children with overweight or obesity (OW/OB). 289 parents (m age=41.4; 86.5% OW/OB; 90.3% female; 48.1% Hispanic, 35.6% Non-Hispanic White) seeking treatment for their child with OW/OB (m age =10.0, 49.1% female, m BMIz=2.1) completed the Comprehensive Feeding Practices Questionnaire (CFPQ), Child Eating Behavior Questionnaire (CEBQ), and demographic questions. Linear regression models evaluated associations between CFPQ subscales (Restriction for Weight Control, Pressure, Child Control, Emotion Regulation, Food as Reward, and Monitoring) and CEBQ subscales (Food Responsiveness [FR] and Satiety Responsiveness [SR]), controlling for parent's BMI, gender, ethnicity, race and age as well as child age, gender, BMIz and family income. Child FR was positively associated with Restriction for Weight Control, Pressure, Emotion Regulation, and Food as Reward (β 's=0.18-0.36, p 's<0.01). Parent BMI and child BMIz were significantly associated with child FR (parent β 's=-0.03 – -0.02; child β 's=0.47 – 0.60) and SR (parent β 's=0.02; child β 's=-0.63 – -0.57) in all models tested (p 's<0.001). Similar to studies in younger children, parent feeding practices and parent and child BMI(z) were related to child FR, but only parent and child BMI(z) were related to child SR. Future studies should evaluate the directionality of these relationships through longitudinal research designs in children with OW/OB.

P112 **The Effects Of Liraglutide On Operant Responding For Food And Social Reinforcers**

Karissa T. Reyes¹, Matthew Preisigke¹, Elizabeth A. Rakowski¹, Brady M. Thompson¹, Luke T. Hannan¹, Leonard H. Epstein², Elizabeth G. Mietlicki-Baase³, Derek Daniels⁴, Paul J. Meyer¹

¹Department of Psychology, University at Buffalo, Buffalo, NY, United States, ²Department of Pediatrics, Jacobs School of Medicine & Biomedical Sciences, Buffalo, NY, United States, ³Department of Exercise and Nutrition Sciences, School of Public Health and Health Professions, Buffalo, NY, United States, ⁴Department of Biological Sciences, University at Buffalo, Buffalo, NY, United States

Liraglutide is a GLP-1 receptor agonist used for the treatment of diabetes and obesity. One possible mechanism to explain the effects of GLP-1 receptor agonists on obesity is a reduction in food reinforcement, as documented by animal studies. In addition, GLP-1 agonists change responding for other reinforcers in humans, including alcohol and smoking. However, the effects of liraglutide on the reinforcing value of healthy behaviors, such as socializing, is unknown. To investigate this phenomenon, rats (N= 60, male= 32, females=28) in two studies were administered either liraglutide or saline vehicle in the context of discrete choice and progressive ratio procedures. During discrete choice trials, rats were able to earn either a palatable food pellet or access to a familiar conspecific, with a screen door opening to allow limited contact. After baseline responding was established, subjects began receiving injections of their assigned drug, with half receiving liraglutide. Dosing schedules differed between the two studies, the first started at 0.1 mg/kg, and escalated to 1 mg/kg, and the second started at 0.025 mg/kg and escalated to 0.3 mg/kg. Progressive ratio tests were administered to assess differences in reinforcer-specific motivation, and discrete choice trials assessed reinforcer preference. Liraglutide induced weight loss as expected, but had only transient effects on responding for food reinforcers in both studies. These results suggest

there is a dissociation of food intake and body weight from food reinforcement measured in operant paradigms.

P113

Factors Predicting Meal Energy Compensation Across Multiple Preload Studies

Barbara J. Rolls, Paige M. Cunningham, Kathleen L. Keller, Liane S. Roe
The Pennsylvania State University, University Park, PA, United States

Preload studies that test the effects of food properties on satiety can have inconsistent results. For this secondary analysis, we combined data from 13 preload studies conducted in our laboratory. The data comprised individual weighed intakes from 2311 meals for 511 participants (63% women; age 18-84 y; BMI 24-48 kg/m²). Our aim was to assess the influence of characteristics of the preload, the test meal, and the participants on both meal energy intake (preload + test meal) and energy compensation (meal energy intake relative to a baseline meal with no preload). Analyses used linear mixed models with repeated measures across individuals. The results show that meal energy intake was affected positively by preload energy, and negatively by preload weight after accounting for energy (both $p \leq 0.0001$). In addition, meal energy intake was positively affected by the amounts served at the test meal, the interval between the preload and test meal, and participant characteristics including sex, BMI, and daily energy needs (but not age). Energy compensation relative to the baseline meal was similarly influenced positively by preload energy and negatively by preload weight (both $p < 0.0001$), but for this relative outcome there was no significant influence of the test meal, interval, or individual characteristics. Overall, complete energy compensation (100%) was found when preload energy was 27% of baseline intake, and preloads with lower values reduced meal energy intake compared to baseline. These findings show the benefit of including a baseline (no-preload) meal from which to calculate a relative measure of energy compensation; this allows researchers to focus on testing preload properties, while accounting for the influence of the test meal and individual characteristics.

P114

Effect Of Nmda Receptors In The Microstructure Of Sodium Intake

ALINE/A ZENATTI^{1,2}, LAURIVAL/A DE LUCA JR², DEREK DANIELS¹

¹UNIVERSITY AT BUFFALO, BUFFALO, NY, United States, ²SAO PAULO STATE UNIVERSITY, ARARAQUARA, Brazil

The antagonism of NMDA-type glutamate receptors using MK-801 temporarily inhibits sodium intake in rats. To further explore this phenomenon, the present study tested if MK-801 affected the microstructure of 0.3 M NaCl intake in rats with sodium appetite. After habituation to access 0.3 M NaCl, rats received an intraperitoneal injection of furosemide. NaCl was withheld and rats were provided only water and a sodium-deficient diet for the subsequent 24 hours. Fifteen minutes before restoring access to NaCl, one group received MK-801 (0.25 mg/kg, i.p.), and the other received vehicle (95% NaCl 0.15 M, 5% DMSO). Access to 0.3 NaCl was restored. Licks for 0.3 M NaCl were monitored continuously for the subsequent 90 minutes and the total volume consumed during the test was determined by the difference in bottle weight from the beginning to the end of the test. Treatment with MK-801 was associated with fewer licks in the first 15 minutes of test, but appeared to increase licking for NaCl after 75 minutes of testing. This difference in lick number was largely a function of the number of bursts; analysis of burst number followed a similar pattern as total licks. Burst size mostly followed the same pattern, but was smaller in the MK-801 group for the first 30 minutes of the test, and did not become larger in the later portion of the test. These data suggest that blockade of NMDA receptors initially decreases the hedonic value of the ingested sodium, while enhancing satiation. Additional studies and analyses are needed to understand the mechanism of the negative feedback that controls sodium intake under these testing conditions.

P115

The Glucagon-Like Peptide-1 Receptor Agonist, Liraglutide, Reduces Opioid Craving And Seeking Behaviors In Rats And Humans

Patricia Sue Grigson¹, Scott Bunce², Timothy Brick³, Christopher Freet², Erin Deneke⁴, Jennifer Nyland¹

¹Department of Neural and Behavioral Sciences Penn State College of Medicine, Hershey, PA, United States, ²Department of Psychiatry and Behavioral Health Penn State College of Medicine, Hershey, PA, United States, ³Department of Human Development and Family Studies Penn State University, Happy Valley, PA, United States, ⁴Department of Psychiatry and Behavioral Health Penn State College of Medicine, Hershey, PA, United States, ⁵Caron Treatment Center, Wernersville, PA, United States

Opioid use disorder (OUD) is a devastating disease, and deaths due to opioid overdose continue to rise. Effective new treatments are needed. We tested the safety and efficacy of a glucagon-like peptide-1 receptor agonist (GLP-1RA) for the treatment of OUD in rats and in humans in residential treatment. **Pre-clinical: Safety.** Treatment with a GLP-1RA did not adversely affect circulating levels of blood glucose or insulin, food intake, bodyweight, motor performance or sleep in rats. **Efficacy.** Treatment with GLP-1RA, administered acutely and/or chronically, reduced drug taking, cue-induced opioid seeking, and drug- and stress-induced reinstatement of opioid seeking in rats. **Clinical: Methods.** In a fully-randomized, double-blind, placebo-controlled study, patients in residential treatment were consented following medically assisted withdrawal, stratified by patient's choice of MAT (buprenorphine) or No MAT, then randomized into placebo (n=10) or liraglutide (n=10) conditions. Liraglutide was administered subcutaneously daily; doses were increased from 0.6 mg to 1.2 mg to 1.8 mg every 6 days, then discontinued on terminal days 20 and 21. **Clinical: Safety.** Daily treatment with liraglutide did not adversely affect body weight, blood glucose, or cardiorespiratory function in this population. **Efficacy.** Data gathered using ecological momentary assessment showed that liraglutide reduced craving compared to placebo (Cohen's d @ .5, $p=0.005$), even at the lowest dose (Cohen's d @ .5, $p=0.005$) and liraglutide, but not placebo, increased the probability among MAT participants of reporting No craving (i.e., precisely 0). **Conclusion.** Although the sample size is small, daily treatment with liraglutide appears safe and effective in reducing craving and seeking in both animals and in humans.

P116

Longitudinal Relationships Between Social Media Use And Binge Eating In The Abcd Study

Xinyi Shi, Sarah Ann Duck, Elena Jansen, Susan Carnell
Johns Hopkins University School of Medicine, Baltimore, MD, United States

Social media use is prevalent in early adolescence, warranting investigation of relationships of excessive use with mental

health including pathological eating behaviors. We used data from the Adolescent Brain Cognitive Development (ABCD) Study, a US-wide cohort of children recruited at 9-11yo, to investigate longitudinal relationships of a child-report measure of social media addiction [SMA], with presence of binge eating symptoms [BE] in the past 2 weeks based on reports from either parent or child. SMA example statements include: "I feel the need to use social media sites/apps more and more" and "I use social media sites/apps so much that it has had a bad effect on my schoolwork or job." Structural equation modelling [SEM] examined relationships between SMA scores and BE at the 2 and 4 year [y] follow-up time-points, and logistic regressions assessed associations of SMA groups (non-addictive vs. moderate vs. severe) at the 2 and 4y follow-ups with BE at the 4y follow-up, adjusting for demographic variables, body mass index [BMI] groups, and BE at the 2y follow-up. Among 2,205 participants with complete data, 13.1% reported BE at the 2y follow-up and 12.3% reported BE at the 4y follow-up. SEM demonstrated a unidirectional relationship, indicating that SMA preceded and contributed to BE, but not vice versa. Logistic regressions demonstrated that SMA at the 2 and 4y follow-ups was associated with BE at the 4y follow-up, and that SMA at the 4y follow-up showed the strongest association with BE at the 4y follow-up. Our findings reveal a prospective association between SMA and BE, and advocate for research using more granular measures of social media use and BE, as well as interventional designs, to evaluate potential effects on pathological eating behavior.

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Vagal Oxytocin Receptors Are Necessary For Normal Esophageal Motility.

Mohammed Asker^{1,2}, Jean-Philippe Krieger^{1,7}, Ivana Maric^{1,2}, Francesco Longo⁸, Stina Bochers^{1,2}, Robert P. Doyle^{3,6}, Matthew R. Hayes⁴, Karolina P. Skibicka^{1,2,5}

¹Department of Physiology/Metabolic Physiology, Institute of Neuroscience and Physiology, The Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden, ²Wallenberg Centre for molecular and translational medicine, University of Gothenburg, Gothenburg, Sweden, ³Department of Chemistry, Syracuse University, Syracuse, NY, United States, ⁴Translational Neuroscience Program, Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States, ⁵Department of Nutritional Sciences, Pennsylvania State University, University Park, PA, United States, ⁶Departments of Medicine and Pharmacology, State University of New York, Upstate Medical University, Syracuse, NY, United States, ⁷Institute of Veterinary Pharmacology and Toxicology, University of Zurich-Vetsuisse, Zurich, Switzerland, ⁸Department of Pharmacology, Institute of Neuroscience and Physiology, The Sahlgrenska Academy at the University of Gothenburg, Sweden., Gothenburg, Sweden

Oxytocin (OT) is traditionally associated with reproductive physiology including its pivotal role in parturition and lactation, but has recently garnered interest for its involvement in modulating feeding behavior. The CNS OT receptors (OTR) have received most attention for their role in OT anorexia. However, we have recently found that peripherally restricted OT can potentially decrease food intake, without inducing food avoidance. Given that OTR are found on the vagus nerve and the well-established role of the vagus in feeding behavior control, the anorexic actions of the peripherally restricted OT suggest the potential role of vagal OTR in feeding behavior control. Therefore, here we evaluated whether vagal OTR are necessary for food intake and body weight control, in male and female rats. Vagal OTR were reduced by virogenetic knockdown bilaterally applied to the nodose ganglia. Surprisingly, we found that the knockdown of nodose OTR did not elicit an increase in body weight or food intake in rats compared to control groups of both sexes. Moreover, nodose OTR knockdown rats, but not controls, exhibited a significantly elevated mortality rate starting 4 weeks after knockdown, with males being disproportionately affected. We observed that mortality followed large eating bouts and was accompanied by abnormal presence of food in the mouth/esophagus, suggesting death by aspiration/food in the airways. Therefore, we hypothesized vagal OTR knockdown changes upper, but not lower, GI tract motility. Terminal experiments revealed a marked accumulation of food within the esophagus of knockdown rats, indicative of impaired esophageal motility. Our findings demonstrate a novel role for the OT system and the essential role of nodose OTR for esophageal peristalsis and swallowing.

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Sexually Dimorphic Monosynaptic Connections Of Bst Mc3R Neurons Are Activated During Feeding And May Drive Divergent Feeding Behaviors

Michelle N. Bedenbaugh, Nicholas T. Low, Haley N. Mendoza-Romero, Richard B. Simerly
Vanderbilt University, Nashville, TN, United States

Previously presented work found melanocortin 3 receptor (MC3R) neurons in the bed nucleus of the stria terminalis (BST) are activated, and can modulate, feeding behaviors and responses to stress. However, sexual dimorphisms are only associated with feeding behaviors and these differences are not due to changes in BST^{MC3R} projections to downstream targets. Thus, the sex differences in feeding behavior may be driven by monosynaptic connections to BST^{MC3R} neurons. To test this, the distribution of cells providing direct inputs to BST^{MC3R} neurons was mapped using monosynaptic tracing, lightsheet imaging and cell registration. Neurons that provide direct inputs to BST^{MC3R} neurons were identified in multiple areas in the hypothalamus, amygdala and cortex. Several areas were found to have significant differences in average cell density between males and females, including the paraventricular hypothalamic nucleus (PVH), median preoptic nucleus (MEPO), lateral hypothalamic nucleus, ventral premammillary nucleus (PMv), paraventricular nucleus of the thalamus and central amygdalar nucleus (CEA). To determine if some of these areas were also significantly activated during feeding, whole brains from animals that were refed after an overnight fast were immunolabeled with Fos, imaged and registered. Multiple areas that send sexually dimorphic inputs to BST^{MC3R} neurons show significant increases in Fos in response to refeeding after a fast, including the PVH, MEPO, PMv and CEA. Altogether, the upstream network of BST^{MC3R} neurons is sexually dimorphic, highly overlapped with brain regions that are activated during feeding and are likely driving the sexually dimorphic feeding behaviors observed when BST^{MC3R} neurons are activated.

P119

Role Of Amygdala Pkr2 Neurons In The Regulation Of Food Intake.

Kate R. Bowman, Ayushi Mittal, Nilufer Saray-Atasoy, Deniz Atasoy, Julien A. Sebag
University of Iowa, Iowa City, IA, United States

The central nervous system plays a critical role in controlling energy homeostasis. Multiple GPCRs and their ligands

modulate neuronal activity to regulate food intake and energy expenditure. Whereas most of our understanding of the central control of feeding focuses on various hypothalamic nuclei, the amygdala is emerging as an important brain region in controlling food intake. In this study, we investigated the role of the Prokineticin Receptor 2 (PKR2) in regulating food intake and body weight. PKR2 is a GPCR coupled to $G_{q/11}$ and regulated negatively by the Melanocortin Receptor Accessory Protein 2 (MRAP2). PKR2 activation by its agonist PK2 is potently anorexigenic. Interestingly, we found that, while PKR2 is expressed both in hypothalamic and amygdala neurons, the anorexigenic response to PK2 is mediated exclusively by amygdala PKR2 neurons. Moreover, our results suggest that PKR2 may play a role in regulating the circadian aspect of food intake since deletion of PKR2 in the amygdala results in daytime hyperphagia. Deletion or overexpression of MRAP2 in PKR2 neurons results in increased or decreased anorexigenic activity of PK2 respectively. Overall, this study identifies the PKR2/MRAP2 complex in amygdala neurons as an important central regulator of feeding behavior.

P120 Octreotide Treatment Increases Meal Size Of A Palatable Cafeteria Diet But Not Of Chow In Female Rats After Roux-En-Y Gastric Bypass

Carolina R. Cawthon¹, Christina N. Boyle², A. Valentina Nisi¹, Ginger D. Blonde¹, Belle Krubitski¹, Carel W. le Roux³, Thomas A. Lutz², Alan C. Spector¹

¹Department of Psychology and Program in Neuroscience, Florida State University, Tallahassee, FL, United States,

²Institute of Veterinary Physiology, University of Zurich, Zurich, Switzerland, ³Diabetes Complications Research Center, Conway Institute, School of Medicine, University College Dublin, Dublin, Ireland

Elevated gut satiation hormones have been detected in humans and rats after Roux-en-Y gastric bypass (RYGB) but it remains unclear how these endocrine changes influence eating behavior leading to intake outcomes. Here, 16 female rats had RYGB or SHAM surgery (8/group). After recovery, we used a novel food choice monitor to assess meal patterns (21 h/d) for 15 d on powdered chow (PC) then 16 d on a custom rodent 5-choice cafeteria diet (CAF). Groups differed in body weight from 4 d post-op until the end of the experiment. During the first 5 d on PC, intake did not differ between the groups, but RYGB rats ate more and smaller meals each day. By the last 4 d of PC, intake and meal patterns were similar between groups. Over the first 10 d of CAF, compared with SHAMs, RYGB rats ate fewer kcal in more frequent but smaller meals. RYGB rats consumed more carbohydrate and less fat than SHAMs, largely because they chose to eat less of the high-fat/high-sugar choice and more of the low-fat/low-sugar choice. After 5 d PC and 10 d CAF, 1 h before food access, rats received the somatostatin analog octreotide (OCT, 100 μ g/kg-BW, SC) or saline in 2-d crossovers to test if enhanced hormonal responses drive the meal pattern differences of RYGB vs. SHAM rats. In RYGB rats, OCT led to increased first-meal size (kcal and g) and duration on CAF but not PC, though 21-h energy intake was reduced on both diets; these measures were unaffected by OCT in SHAMs on PC or CAF. In SHAMs on CAF, OCT significantly but modestly reduced 21-h meal number but did not affect meal patterns of RYGB nor alter food choices in either group. These results suggest that enhanced hormonal responses mediate the reduction in meal size in female rats after RYGB when palatable diets are offered but not on standard chow.

P121 A History Of High-Fat Diet Alters Reward Processing And Dopamine Signaling In The Nucleus Accumbens.

Claire Corbett, Brianna Linneman, Leighelle Adrian, Timothy Sloand, Mark Niedringhaus, Elizabeth West
Rowan University, Stratford, NJ, United States

With the increased prevalence of consumption diets high in fat in modern societies, it is critical to consider the effects on brain function and behavior. Here, we aimed to determine the effects of a high-fat diet on reward processing and dopamine (DA) signaling in the nucleus accumbens (NAc). Male and female Long-Evans rats were divided into a control group fed a standard chow diet (n=7) and an experimental group fed a high-fat diet (n=8) for 12 weeks. At week 10, we measured rats' preference for high-concentration sucrose (12 %) compared to low-concentration sucrose (4 %) for 7 daily sessions. We found that the rats fed a high-fat diet consumed less of a high sucrose concentration compared to control rats. Following the preference tests, rats underwent stereotaxic surgery to inject the genetically encoded GPCR-activation-based-DA (GRABDA) and optical ferrules into the NAc. Rats underwent 15 days of Pavlovian conditioning in which one cue predicted a sucrose pellet (CS+) and a different cue did not (CS-) to evaluate learning while measuring NAc dopamine dynamics using fiber photometry. We found that both groups spent more time in the food cup the CS+ (chow: 18.5% +/- 4.4; high-fat diet: 11.3%) compared to the CS- (chow: 13.3% +/- 4.3%, high-fat: 3.7% +/- 2.2) indicating intact associative learning. However, behavioral responses to the cues were diminished in rats fed the high-fat diet (i.e., they spent less time in the food cup during both cues) compared to control rats (main effect of diet, p=0.0005). Also, rats exposed to the high-fat diet exhibited an abolishment of NAc dopamine signaling during reward-predictive cues but intact dopamine dynamics (increase) to the reward. Thus, a history of high-fat diet alters reward processing and NAc dopamine signaling.

P122 Sex Differences In Dopaminergic Encoding Of Food Reward

Asia Dofat, Alec Hartle, Katie Marschalko, Rachelle Jacob, Keyrstin Jacobs, William Howe
Virginia Tech School Of Neuroscience, Blacksburg, VA, United States

The nutrient content of food significantly influences its reward value. Recent research highlights a pathway linking gut nutrient sensors to brain dopamine (DA) systems as key in this process. Previous work has demonstrated that both food reward and DA release dynamics differ between males and females, however, little is known regarding sex-specific variations in DA release and relationship to food reward. Here, we first assessed food preference daily, for two weeks, using a three-choice free feeding task while sucrose, fat, and a combination of fat and sucrose ('combo') were freely available in male and female mice. Males (n=18) consumed mostly combo across the two-week testing period, whereas females (n=22) showed a strong preference for fat. Experiments using fiber photometry and the DA sensor dLight1.1 revealed that this preference corresponded with sex-specific patterns (n=3

male and n=4 female) of nucleus accumbens DA release. We explored the potentially mediatory role of estrous cycle on food preference, and found that fat preference remained consistent throughout the cycle. Although females consumed more calories from fat, like males, during preference tests they approached the combo food first, suggesting some aspects of reward were preserved across sexes. We next tested the ability of fat and combo to create a conditioned place preference. Whereas combo created a place preference over fat in males (n=6), the reverse pattern was observed in females (n=5). Our combined data suggest fat and combo foods are differentially reinforcing in males and females, and this is reflected at the level of terminal DA release. Ongoing experiments are exploring the post-ingestive effects of these foods directly using intra-gastric infusions and cfos immunohistochemistry.

P123

A Visceral Neuroimmune Circuit Modulates Satiation And Tempers Colitis-Induced Bodyweight Loss

Payam A Fathi, Jessica E Biddinger, Julio E Ayala
Vanderbilt University School of Medicine, Nashville, TN, United States

Nucleus of the solitary tract (NTS) neurons respond to- and integrate visceral signals. Preproglucagon neurons (NTS^{PPG}) are glutamatergic NTS neurons and play a distinct role in regulating satiation. A subset of NTS^{PPG} neurons express the interleukin-6 receptor (IL-6R) and functionally respond to the inflammatory cytokine IL-6, however the physiological relevance of this signaling is unknown. Using metabolic phenotyping we showed that PPG neuron IL-6R knockout (PPG^{IL6R-KO}, PPG^{Cre} x IL-6R^{f/f}) and wild-type (WT^{IL6Rf/f}) mice are identical at baseline. However, when fed a chronic 60% high-fat diet (HFD), which elevates IL-6 levels, WT^{IL6Rf/f} but not PPG^{IL6R-KO} mice increase per-meal calorie consumption suggesting a diet dependent, IL-6 mediated, impairment in satiation. Longitudinal caloric preload satiety tests during HFD feeding showed that PPG^{IL6R-KO} mice significantly retained sensitivity to caloric preload further demonstrating a mechanism through which IL-6 impairs the ability of NTS^{PPG} neurons to regulate satiety/satiation. Since NTS^{PPG} neuron IL-6R signaling during sub-chronic elevations in IL-6 increased meal specific caloric consumption we hypothesized that these changes in satiation may enhance fitness during infections. DSS-induced colitis significantly decreased meal sizes and exacerbated weight-loss in PPG^{IL6R-KO} mice. Loss of peripheral neuron derived IL-6 (PNS^{IL-6KO}, Na_v1.8^{Cre} x IL-6^{f/f}) was sufficient to recapitulate the exacerbated colitis-induced bodyweight loss. Our findings describe a periphery-to-NTS neuroimmune circuit sensing visceral organ inflammation and modifying feeding behaviors to convey a fitness advantage by dampening infection-associated excess bodyweight loss.

P124

Semaglutide Decreases Binge-Like Eating In Female Rats.

Daniel, M. Gaines, Jamila, R. Guard, Lisa, A. Eckel
Florida State University, Tallahassee, FL, United States

Semaglutide (SEMA) is effective in decreasing palatable food intake, leading to weight loss, in individuals with obesity. Less is known about its ability to decrease binge eating in bulimic syndromes. Here, we tested the hypothesis that SEMA would decrease the overconsumption of calories in a rodent model of binge-like eating. To induce binge eating, female rats were maintained on chow and given intermittent access to high fat diet (HFD) at 4-day intervals (INT group). Control groups had free access to chow or chow and HFD (CHOW and HFD groups). Within these diet groups, rats received daily injection of SEMA (70 µg/kg) or vehicle. We further assessed SEMA's ability to decrease hedonic eating within a 30-min chocolate Ensure "dessert" test, administered immediately after the consumption of a satiating meal. During the binge eating phase of the study, daily caloric intake was decreased in INT and HFD rats, relative to CHOW rats. When HFD was available, INT rats consumed 30-40% more calories (i.e., binged) during the first 2h of the dark phase than control groups. SEMA decreased food intake on binge days in INT rats (62.9 ± 3.8 vs 40.2 ± 5.1 kcal/2h) but did not alter food intake during the same 2-h interval in CHOW or HFD rats (9.9 ± 3.1 vs 7.1 ± 2.4 kcal/2h). During the dessert test, SEMA decreased chocolate Ensure intake by 40-50% in HFD and INT rats but had no effect in CHOW rats. SEMA was also more effective in decreasing fat mass (assessed via EchoMRI) in INT rats, relative to HFD and CHOW rats. We conclude that SEMA decreases binge-like and hedonic eating in female rats with prior exposure to HFD. Ongoing analyses are examining whether these effects of SEMA are mediated by its ability to increase meal-stimulated satiation signals.

P125

How Does Kir7.1 Intricately Regulate The Response Of Paraventricular Hypothalamus (Pvh) Neurons?

Ciria Hernandez, Naima Dahir, Luis E Gimenez, Roger Cone
University of Michigan. Life Science Institute, Ann Arbor, MI, United States

The regulation of energy homeostasis involves the interplay between α -melanocyte stimulating hormone (α -MSH) and Agouti-related protein (AgRP) acting on the melanocortin-4 receptor (MC4R) in the paraventricular nucleus (PVH) of the hypothalamus. Traditionally thought to operate through a *Gas* signaling pathway, recent findings reveal a novel mechanism where α -MSH couples MC4R to Kir7.1 potassium channels, modulating PVH neural firing. Conversely, AgRP induces Kir7.1 channel opening, inhibiting PVH neuron activity. This dual regulation suggests that MC4R may control PVH neurons via both G-protein signaling and Kir7.1 activity. Blocking Kir7.1 led to reduced food intake and weight loss, mimicking α -MSH effects while nullifying AgRP's food intake promotion. Unexpectedly, combining AgRP with the Kir7.1 blocker reduced food intake compared to either alone. Kir7.1 inhibition increased MC4R agonist responsiveness, specifically in PVH neurons, highlighting the physiological role of Kir7.1 in energy homeostasis and shedding light on MC4R's unique characteristics.

P126

Examining The Protective Effects Of Estrogen For Binge Eating During Adolescence.

Alex Johnson¹, Cheryl Sisk¹, Kristen Culbert¹, Pence Nathan¹, Jenna Lee¹, Lauren Raycraft², Kelly Klump¹

¹Michigan State University, East Lansing, MI, United States, ²University of Michigan, Ann Arbor, MI, United States

Prevalent forms of eating disorders are those characterized by binge eating (BE), which reflects consumption of a large amount of food in a short period of time, with a loss of control over the eating episode. Little is known about the etiology of BE or the biological factors that contribute to its female predominance. Ovarian hormones are key biological candidates to consider as they become elevated during puberty in females and drive physical and neural development during this key phase of development. Moreover, lower levels of estrogen are associated with increased risk for BE in females; however, it is currently unknown whether pubertal exposure to estrogen provides organizational effects that protect against the development of BE. In this study, we used an animal model of individual differences in binge eating to examine the organizational effects of ovarian hormones on risk for BE in female rats and tested the hypothesis that pubertal exposure to estrogen provides protection against the onset of BE. We employed remove and replace hormone paradigms, in which prepubertal female rats (P25) received either sham surgery, ovariectomy with estradiol benzoate replacement, or ovariectomy without hormone replacement. Upon recovery, rats received intermittent access to palatable food (PF) 3x/week for eight weeks to identify binge eating prone (consistently high levels of PF intake) and resistant (consistently low levels of PF intake) rats. A separate cohort of female rats also received intermittent access to PF following either prepubertal sham surgery, or ovariectomy; however, estrogen replacement occurred in adulthood. Overall, these studies will determine whether the pubertal period is a developmental window of sensitivity to estrogen-dependent protection against BE.

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Insulin Modulates Excitatory Drive Of Pyramidal Neurons In The Posterior Piriform Cortex.

Vaibhav R. Konanur, Celine Sanluecha, Lindsay R. Vivona, Joseph D. Zak
University of Illinois at Chicago, Chicago, IL, United States

Olfactory cues in the environment can signal food availability. Odors associated with nutritive substances initiate anticipatory physiological changes, including cephalic phase insulin release (CPIR). CPIR is a strong driver of food intake and modulates odor perception. However, little is known about the mechanism through which CPIR modulates odor processing. To address this question, we applied insulin ($1 \mu\text{g}\cdot\text{ml}^{-1}$) to acute coronal tissue slices of the posterior piriform cortex (PPC; AP: +0.1 mm) while recording from voltage-clamped pyramidal neurons ($n = 7$). At -70 mV , the average instantaneous frequency ($\beta = -2.30$, $p < 0.01$) and the average amplitude of spontaneous excitatory postsynaptic currents (EPSC; $\beta = -1.45$, $p < 0.01$) decreased. However, the effects of insulin were heterogeneous. Insulin increased the instantaneous EPSC frequency in a subset of neurons (43%), and it decreased in a separate subset of neurons (43%). Similarly, 29% of neurons had larger EPSC amplitudes following insulin application, while in another 29% of cells, EPSC amplitudes were decreased. The satiety factor, glucagon-like peptide 1 (GLP-1) has been shown to modulate insulin signaling in the olfactory system. Therefore, we hypothesized that hindbrain GLP-1 neurons in the nucleus of the solitary tract (NTS) project to the PPC, where they can modulate pyramidal cell excitability. We injected a retrograde fluorescent tracer, cholera toxin subunit b (CTb), into the PPC. We indeed observed neurons containing CTb in the NTS, thereby indicating a direct connection between the NTS and PPC. Future studies will identify the peptidergic contents and functionality of these neurons. Our data suggest the possibility of NTS GLP-1 neurons projecting to the PPC to modulate olfactory processing.

P128

Satiety Liver/Foregut Hormone Leap2 Does Not Correlate With Non-Food Reward Anticipation Or Delay Discounting, Motor Response Inhibition Nor Trait Impulsivity In Adults With Obesity

Marguerite Leoni¹, Raghav Bhargava¹, Mimoza Emini¹, Marcela Rodriguez Flores¹, Navpreet Chhina¹, Eleanor Brian¹, Rioghnach Hannan¹, Ghadah Aldubaikhi¹, Madhawi Aldhwayan², Werd Al-Najim³, Aruchuna Ruban⁴, Michael A Glaysher⁵, Christina G Precht⁶, James P Byrne⁵, Julian P Teare⁴, Anthony P Goldstone¹

¹PsychoNeuroEndocrinology Research Group, Division of Psychiatry, Department of Brain Sciences, Imperial College London, London, United Kingdom, ²Community Health Sciences Department, King Saud University, Riyadh, Saudi Arabia, ³Department of Metabolism, Diabetes and Reproduction, Imperial College London, London, United Kingdom, ⁴Department of Surgery and Cancer, Imperial College London, London, United Kingdom, ⁵Division of Surgery, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom, ⁶Clinical Trials Unit, Department of Public Health, Imperial College London, London, United Kingdom

Background: The liver/gut satiety hormone LEAP2 is an inverse agonist at the acyl ghrelin (AG) GHSR receptor. GHSR signalling via midbrain dopaminergic neurons is important in eating/addictive behaviours. There is some evidence for stimulatory effects of AG on impulsivity to food in rodents and non-food rewards in humans, and variable effects of AG or fasting on monetary reward processing in humans. **Hypotheses:** Endogenous plasma LEAP2 negatively correlates with brain responses during monetary reward anticipation, motor response inhibition, and measures of temporal and trait impulsivity. **Methods:** Overnightfasting plasma LEAP2 in $n=41-43$ adults with obesity (31-64 years, 63-65% female, 77-78% T2DM, BMI $31-55 \text{ kg/m}^2$), completing monetary incentive delay (MID) and non-food Go/NoGo (GNG) fMRI tasks, was correlated with BOLD signal in fROIs (MID: striatum, anterior insula, amygdala, vACC, OFC; GNG: dlPFC, IFG, ACC, insula, putamen, SMA, pre-SMA). Fasting plasma LEAP2 was also correlated with delay discounting rate (DDR) for money and trait impulsivity questionnaires in expanded cohort of $n=93$ adults with obesity. **Results:** There were no significant correlations of fasting plasma LEAP2 with: (i) BOLD signal during monetary reward anticipation in MID fMRI task, (ii) task performance or BOLD signal during successful inhibition in GNG fMRI task, (iii) DDR for money, nor (iv) BIS-11 or UPPS-P impulsivity questionnaires ($P > 0.05$). **Conclusion:** The lack of significant correlations with fasting plasma LEAP2 does not yet support a role for GHSR signalling on non-food reward anticipation or impulsivity in obesity. Correlations with fasting plasma AG/LEAP2 ratio and whole brain fMRI analyses are ongoing, to further investigate the potential role of GHSR in these addictive behaviours.

P129

Kcnk13 Channel Mediates Glucose-Sensing And Hfd-Induced Activation In Microglia

Qingzhuo Liu, Hailan Liu, Jonathan C. Bean, Xing Fang, Yongxiang Li, Yue Deng, Longlong Tu, Mengjie Wang, Yuxue Yang, Na Yin, Junying Han, Yongjie Yang, Yang He, Chunmei Wang, Yong Xu
Baylor College of Medicine, Houston, TX, United States

Microglia play a crucial role in energy metabolism and its dysfunction results in many metabolic disorders. A previous study

suggests that high-fat-diet (HFD) exposure triggers microglia activation and hypothalamic inflammation, but the underlying mechanism responsible for this response remains unclear. Here, we show that HFD induces hyperpolarization of microglia in the arcuate nucleus of the hypothalamus (ARH), which is associated with increased KCNK13-mediated potassium outward currents. Through brain slice electrophysiological recording, we show that the increase of extracellular glucose level enhances KCNK13 currents in ARH microglia, leading to the microglia hyperpolarization, which mimics the effects of HFD. Tetrapentylammonium (TPA), a selective KCNK13 channel blocker blunts the microglia hyperpolarization induced by high glucose level. Interestingly, perfusion of TPA to the brain slices activates POMC neurons, while TPA puff towards POMC neurons has no effects. Since KCNK13 is exclusively expressed in microglia, our findings suggest potential interactions between microglia and surrounding POMC neurons. Further, we show that intraperitoneal injections of TPA significantly suppresses food intake and body weight gain in both chow and HFD-fed mice. In summary, our findings suggest that KCNK13 mediates glucose-sensing and activation in microglia in the context of obesity, and inhibition of KCNK13 in microglia can rescue the diet-induced obesity possibly via activating POMC neurons.

P130

Reduction In Excitatory Presynaptic Drive Is Associated With Changing Dopamine Responses To Sucrose In A Conditioned Taste Aversion Paradigm

Maxine K. Loh^{1,2}, Sean Schrank², Josh Sevigny², Samantha Hurh², Dennis R. Sparta², Mitchell F. Roitman^{2,3}

¹Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of Illinois at Chicago, Chicago, IL, United States, ²Department of Psychology, University of Illinois at Chicago, Chicago, IL, United States, ³Graduate Program in Neuroscience, University of Illinois at Chicago, Chicago, IL, United States

Ingested stimuli resulting in illness are remembered and subsequently avoided (conditioned taste aversion; CTA). Dopamine release in the nucleus accumbens (NAc), driven by ventral tegmental area dopaminergic (VTA_{DA}) neuronal firing, is key for encoding food reward. How dopamine encoding changes for initially rewarding tastes linked to negative post-ingestive outcomes is unclear. Here, we expressed GRAB_{DA2h} in the NAc or cre-dependent GCaMP6s in the VTA of TH Cre+ rats to capture real-time dopamine release and VTA_{DA} activity, respectively via fiber photometry. Separately, we delivered cre-dependent tdTomato to the VTA of TH Cre+ subjects to fluorescently tag VTA_{DA} neurons. Brief (5s; 200 μ l) intraoral infusions of 0.3M sucrose (30 trials/session; 35-55s intertrial interval) were delivered. Rats were then injected (conditioning) with malaise-inducing LiCl (Paired) or saline (Unpaired). The next day, rats received the counterbalanced injection without sucrose infusions and were untreated the following day. This 3-day process was repeated twice. Photometry results revealed that sucrose-evoked dopamine release and VTA_{DA} activity were unchanged in Unpaired, but increasingly suppressed in Paired rats across conditioning days. To assess VTA plasticity, in vitro recordings of spontaneous post-synaptic currents (PSCs) from VTA_{DA} neurons were made after conditioning. While the amplitude of PSCs was unaffected, excitatory PSC frequency was reduced in cells from Paired relative to Unpaired rats, indicative of weakened presynaptic excitatory drive. These results implicate plasticity of excitatory inputs onto VTA_{DA} neurons in the flip from increased to decreased dopamine responses to sucrose in CTA. Ongoing work aims to identify the source(s) changing excitatory drive.

P131

Brain Stimulation Reward Supports High Discriminability And Stable Responding In Probabilistic Discounting Tasks Relative To Sugar Pellet Reward

Deaglan A McAndrew, Sema M Patel, Rachel M Donka, Jamie D Roitman
University of Illinois Chicago, Chicago, IL, United States

Probabilistic discounting (PD) tasks measure reward processing and risk taking, determining the depreciation of perceived reward value based on the probability of reward delivery. To assess PD, subjects choose between smaller-certain and larger-uncertain reward options. Rodents typically engage in tasks for food rewards. However, food restriction is necessary to ensure engagement and motivation declines across the session as satiety develops. By contrast, brain stimulation reward (BSR) is a highly discriminable non-satiating reward. We sought to compare BSR with sugar pellet reward in PD tasks. Rats (n=10) were implanted with stimulating electrodes in the medial forebrain bundle and trained to lever press for BSR. Using a rate-frequency protocol, we determined the threshold (theta-0%) and maximal (alpha-100%), stimulation frequencies. We used intermediate frequencies (25, 50, and 95% of alpha) for the PD task. After confirming discrimination of BSR frequencies (e.g. 95vs50%), rats performed a PD task with 5 blocks of decreasing larger reward probability (p=1.0, 0.8, 0.6, 0.4, 0.2). We systematically varied BSR frequencies to determine the relationship between value and risk preference. Following BSR PD, subjects were food restricted and shaped to lever press for sugar pellets. After confirming reward discrimination (3vs1 pellets) they performed the PD task. Overall, BSR required fewer training sessions to attain stability, supported higher discriminability, and greater preference for larger reward. In PD, preference for the larger reward declined as probability decreased. This supports the use of BSR in PD tasks. To avoid food restriction and within-session satiety, BSR can provide a method to determine the contributions of physiological manipulations to decision making

P132

The Estrogenic Reduction Of Water Intake Stimulated By Dehydration Is Not Associated With An Elevation In Excitatory Cell Activation In The Subfornical Organ.

Lasni Nishshanke, Andrea Edwards, Jessica Santollo
Department of Biology, University of Kentucky, Lexington, KY, United States

Estradiol's (E2) inhibition of water intake has been well documented, yet the underlying mechanisms changing this behavior remain unclear. E2 treatment decreases water intake in female rats following water deprivation. To further understand this effect, this study investigated the associated drinking microstructure changes and explored whether E2 modulates the activation of excitatory cells in the SFO, which are associated with stimulating drinking, during dehydration. Ovariectomized rats were administered estradiol benzoate (EB) and underwent 24 hours of water deprivation. Water intake and licks were monitored for 2 hours to assess behavioral responses. In a second group of rats, brains were extracted and processed for FOS and CaMKII to examine neuronal activity in the excitatory cells in the SFO. As expected, EB treatment reduced intake compared to oil controls. This occurred through a decrease in burst number (p < 0.05), while burst size remained unaffected. Also as expected, water deprivation increased FOS expression in the SFO, and water-deprived rats exhibited a higher number of CaMKII cells expressing FOS (p < 0.05). This response, however, was mediated by the oil-treated rats. EB-treated rats showed no elevation in FOS expression in the CaMKII cells. This, however, was unexpectedly due to an increase in activation of CaMKII cells in the non-deprived state. Despite EB decreasing water intake in water

deprived rats, corresponding excitatory cell activation was not significantly different between the two groups. The decreased burst number in EB-treated rats suggests that E2 influences water intake through alterations in post-ingestive signaling, indicating that satiety signals, instead of the CaMKII cells that drive intake, may be the target of E2.

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Interactions Between Circulating Glp-1 And Hypothalamic Signaling Predict Weight Change In Young Adults

Sandhya P. Chakravarti^{1,2}, Ralf Viet³, Alexandra G. Yunker¹, Brendan C. Angelo¹, Kay Jann⁴, John R. Monterosso^{2,5}, Stephanie Kullman³, Kathleen A. Page^{1,2}

¹Keck School of Medicine, USC, Los Angeles, CA, United States, ²Neuroscience Graduate Program USC, Los Angeles, CA, United States, ³Institute for Diabetes Research and Metabolic Diseases of the Helmholtz Center Munich at the University of Tübingen, Tübingen, Germany, ⁴Mark & Mary Stevens Neuroimaging & Informatics Institute, USC, Los Angeles, CA, United States, ⁵Department of Psychology, USC, Los Angeles, CA, United States

This study aims to evaluate the impact of peripheral glucagon-like peptide-1 (GLP-1) and hypothalamic signaling mechanisms on longitudinal weight changes in young adults. 35 adults (51% female; 23±4 years) with healthy weight, overweight, or obesity underwent perfusion MRI and blood sampling before and after glucose (75g) ingestion to test the effects of changes in hypothalamic blood flow and circulating GLP-1 levels on longitudinal weight change. Hypothalamic blood flow (measured by arterial spin labeling) and circulating GLP-1 were measured fasting, +15, +30min after glucose ingestion. GLP-1 was additionally measured at 120 min after glucose ingestion. Weight was measured the day of the experiment and self-reported approximately 6 months after the experimental session. Linear regressions were used to examine associations between peripheral GLP-1 levels, hypothalamic responses, and weight change. Models were adjusted for age, sex, ethnicity, and BMI. The hypothalamic blood flow response to glucose (normalized to baseline and corrected for whole brain blood flow) was -.41 to .44. GLP-1 AUC was 101.7 to 6307.1 pg/mL*min, and circulating GLP-1 peaked 15 minutes after oral glucose. Weight change over 6 months was 1.4 ± 11.3 lbs, and 54% gained weight while 46% lost weight. Neither circulating GLP-1 nor hypothalamic response to glucose individually predicted weight change. However, there was a significant interaction between circulating GLP-1 and hypothalamic response to glucose predicting changes in body weight ($p < .019$). For individuals with the lowest tertile of circulating GLP-1 levels, there were positive associations between changes in the hypothalamic response to glucose and weight gain ($\beta = 50.9$, $p < .006$). There were no associations between change in hypothalamic blood flow and weight change in individuals with the middle, or highest tertile of GLP-1 levels. Our results suggest that the concurrent response between GLP-1 levels and hypothalamic signaling is a more robust predictor of body weight change than examining brain or periphery signals individually.

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Additive, Non-Intersectional Action Of Hypothalamic Hunger Circuits Overcomes Cost For Acquisition Of Food

Ryan J Post^{1,2}, Morgan Kindel¹, Nitsan Goldstein¹, Nicholas K Smith¹, Rachael Villari¹, Jamie R E Carty¹, Kayla A Kruger¹, Lukas Richie¹, Bridget Skelly¹, Emma N Morley², Claire O Kelly², J Nicholas Betley¹

¹University of Pennsylvania, Philadelphia, PA, United States, ²Providence College, Providence, RI, United States

Adaptive behavior requires changing behavioral strategies based on the relative cost of each action. Such behavioral plasticity is essential for survival, yet how the brain influences these calculations is not fully understood. To model how food consumption changes in a dynamic world, we used multiple assays that impose different and quantifiable environmental or energetic costs to obtaining food and then assessed consumption. We found that hunger drives mice to overcome significant costs to obtain food, and that the behavioral effects of hunger are completely recapitulated by activity in arcuate nucleus (ARC) Agouti-related peptide (AgRP)-expressing neurons. Optogenetically activating individual AgRP neuron projections does not lead to the same behavioral shifts observed in hunger. However, simultaneously activating multiple AgRP subpopulations demonstrates that AgRP projections are additive in their ability to increase motivation to obtain food as cost increases. Using calcium imaging, we find that hunger does not inhibit signals of environmental cost in AgRP projection target regions. Instead, this information is relayed to cortical ensembles and the emergence of behavior correlates with the relative strength of each individual need. Taken together, these findings demonstrate that the previously observed redundancy in hunger networks is necessary to increase 'hunger pressure' that ensures food intake when the cost of obtaining food is high. Our data suggest the unanticipated conclusion that adaptive food intake occurs not through the selective filtering of competing signals of need, but rather by a simultaneous weighting of the two needs that shifts cortical activity to feeding-specific ensembles in situations of starvation.

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Enhanced Food-Cue Responsivity In Obesity Prone Rats: Contributions Of Medial Prefrontal Cortex Inputs To The Nucleus Accumbens

Lauren M Raycraft¹, Finn Seibold², Carrie Ferrario^{1,2}

¹Department of Pharmacology, University of Michigan, Ann Arbor, MI, United States, ²Department of Psychology, University of Michigan, Ann Arbor, MI, United States

Studies in rodents indicate that innate differences in Pavlovian motivation and striatal function contribute to susceptibility for obesity, even prior to weight gain. For example, in selectively bred obesity prone (OP) and resistant (OR) rats, OP males show enhanced sensitivity to food-paired cues compared to OR rats in a Pavlovian to instrumental transfer (PIT) task. In this task, rats learn to associate a cue (conditioned stimulus, CS+) with food (unconditioned stimulus, US) and in separate sessions learn to lever press for US delivery. During testing, the ability of the CS+ to invigorate active lever responding despite no US delivery is measured and indicates the ability of the CS to invigorate food-seeking. Enhanced PIT in OPs was associated with increased expression of calcium-permeable AMPA receptors (CP-AMPA) and was blocked by selective antagonism of CP-AMPA receptors in the nucleus accumbens (NAc) (Derman & Ferrario, 2018). Additionally, inhibition of medial prefrontal cortex (mPFC) inputs to the NAc is sufficient to increase CP-AMPA transmission in males (Fetterly et al., 2023), suggesting that reductions in mPFC activity may enhance PIT. We will present results from ongoing studies examining effects of in vivo DREADD-mediated inhibition of mPFC inputs to the NAc on PIT and NAc CP-AMPA. Furthermore, PIT behavior in our model has been examined exclusively in males. Therefore, we will determine whether OP females also show enhanced PIT compared to ORs. In addition, we are developing a novel conditioned reinforcement task to further investigate Pavlovian incentive motivation in these animals. Altogether, these studies will provide important insight into the neurobiology of motivation during PIT, as well as potential sex differences in obesity prone populations.

The Laterodorsal Tegmental Nucleus Suberves Learned Nutrient Preference

Ciorana Roman Ortiz¹, A-Hyun Jung², Leah J. Wootton², Badruddin Mahamed³, Kieran Heung², Amelia Cave⁴, Jack Brown², Benjamin Phan², Lindsey A. Schier^{1,2}

¹Human and Evolutionary Biology, Department of Biological Sciences, University of Southern California, Los Angeles, CA, United States, ²Neuroscience Graduate Program, University of Southern California, Los Angeles, CA, United States,

³Quantitative Biology, Department of Biological Sciences, University of Southern California, Los Angeles, CA, United States, ⁴Health and Human Sciences, Department of Sociology, University of Southern California, Los Angeles, CA, United States

The laterodorsal tegmental nucleus (LDTg) is a brainstem structure involved in reward and aversion, but whether the LDTg mediates these opposing processes in relation to food stimuli remains unknown. We previously showed that ingestive experience with metabolically-distinct sugars, glucose and fructose, simultaneously enhanced glucose's appeal and attenuated fructose's appeal, suggesting that nutritive conditioning can involve bidirectional changes in valence. In a brain-wide mapping study, we found that sugar-conditioned mice had differential c-Fos responses to glucose and fructose in the LDTg, while unconditioned mice did not. Moreover, chemogenetic silencing of LDTg attenuated the learned preference for glucose, owing to a selective increase in licking for fructose. These findings suggest that the LDTg mediates the selection of the nutritionally-advantageous glucose by promoting the inhibition of prepotent responses to the more palatable sugar (fructose). In line with this, LDTg silencing during fructose intake altered neuronal (c-Fos) activity in periaqueductal gray and central amygdala, revealing its functional connectivity to other key structures associated with avoidance. We thus evaluated if LDTg activity is required for unconditioned and/or conditioned taste avoidance. LDTg silencing did not affect licking responses for an aversive quinine solution, nor did it affect intake of a palatable solution that was paired with lithium chloride-induced malaise. In ongoing studies, we are using *in vivo* imaging to track changes in LDTg activity with sugar conditioning, and investigating if the LDTg is involved in reward devaluation aspects of nutrient learning. The collective findings provide new insights into the neurobehavioral processes underlying food preferences.

RTIOXA-47, A Dual Orexin Receptor Agonist, Increases Energy Expenditure And Decreases Fat Mass In Obesity-Prone Rodent Models

Carolina L Sandoval-Caballero¹, Vijay Mavanji^{1,2}, Miranda Ward^{1,2}, Laurie Shekels^{1,2}, Brianna Pomonis², Yanan Zhang³, Catherine M Kotz^{1,2}

¹Department of Integrative Biology and Physiology, University of Minnesota, Minneapolis, MN, United States, ²Research Service, Minneapolis VA Health Care System, Minneapolis, MN, United States, ³RTI international, Research Triangle Park, Research triangle park, NC, United States

Orexins are neuropeptides that bind to G-protein coupled receptors 1 and 2 in brain regions that regulate body weight (BW) and energy expenditure (EE). In rodents, orexins increase physical activity (PA) and EE. We hypothesized that a synthetic dual orexin receptor agonist RTIOXA-47 prompts BW loss by increasing EE and decreasing fat mass (FM) in rodents. To test this, we injected RTIOXA-47 intraperitoneal and assessed its effects on PA, EE, food intake (FI), and FM in obesity-prone (OP) rats and New Zealand obese (NZO) mice. We showed that RTIOXA-47 (40mg/kg): (1) increased PA without affecting FI, (2) increased 24h EE in OP rats, (3) decreased BW, and (4) decreased FM in NZO mice. These data suggest that RTIOXA-47 could maintain reduced BW after BW loss and prevent BW gain after re-feeding in diet-induced obese mice. To test this, we are feeding male and female mice with a high-fat diet (HFD, D1245, research diets) to induce obesity. Then, half of these HFD-fed mice will be calorie-restricted to induce weight loss (weight gain/loss group), and the other half will be fed ad libitum with HFD (weight gain group). We will inject RTIOXA-47 in both groups, and SPA, EE, BW, and FM will be measured. Preliminary data show that lean mass positively correlates with BW in males ($R=0.96$, $p<0.05$) and females ($R=0.97$, $p<0.05$). Females fed with a high-fat diet (HFD) gain weight faster than HFD-fed males, and we will treat each set of animals with RTIOXA-47 once a 20% increase in BW relative to low-fat diet-fed controls. Studies are in progress, but we predict that RTIOXA-47 will increase PA and EE as well as RTIOXA-47 will decrease FM and maintain the post-weight loss BW in HFD mice. Together, these data highlight the therapeutic potential of orexin agonists to treat obesity.

Astrocytic Melanocortin-4 Receptors In The Paraventricular Nucleus Of The Hypothalamus Are Novel Regulators Of Neuroinflammation And Weight Regulation In Mice

Amanda Sharpe, Adrianna De Santis, Laci Liter
University of Oklahoma Health Sciences, Oklahoma City, OK, United States

The goal of the current study was to determine if rescue of melanocortin 4 receptors (MC4R) on astrocytes in the paraventricular nucleus of the hypothalamus (PVN) in MC4R null mice attenuates obesity and neuroinflammation. Melanocortins acting on MC4R are essential mediators of weight homeostasis by mediating feeding and metabolism. Although the prevailing assumption is that neuronal MC4R are solely responsible for weight homeostasis, astrocytes also express MC4R (aMC4R) which published work suggests are anti-inflammatory. Hypothalamic inflammation induces hyperphagia and correlates with obesity, so we hypothesized that the aMC4R regulate body weight homeostasis through inhibiting inflammation. Work from our lab showed that selective deletion of aMC4R in the medial hypothalamus increases inflammation, weight gain, and adiposity. Here, MC4R null mice (loxTB Mc4r, n=23) were injected bilaterally into the PVN with an AAV-GFAP (astrocyte-specific promoter) vector to express either Cre-GFP (rescue) or eGFP (control). Male mice with aMC4R rescue showed attenuated weight gain compared to controls, however female mice showed no difference in body weight between groups. Acute feeding studies conducted at approximately 3 weeks post AAV injection showed that acute administration of MC4R agonist setmelanotide (3.6 $\mu\text{mol/kg}$) did not significantly alter food intake in either group of mice, suggesting that agonist activity on aMC4R is not directly capable of mediating food intake. Immunohistochemical analysis of inflammatory markers showed a decrease in inflammation following aMC4R rescue. This work identifies aMC4R as novel regulators of body weight homeostasis, likely via effects on hypothalamic inflammation.

Neurotensin In The Lateral Hypothalamic Area Is Necessary For Control Of Body Weight And Antinociception

Katie Thompson, Raluca Bugescu, Rabail Khan, Geoffroy Laumet, Gina Leininger

Injecting neurotensin (Nts) peptide into the brain reduces feeding and provides antinociception but the endogenous sources of Nts mediating these effects are unclear. Activating neurons in the lateral hypothalamic area (LHA) that co-express Nts and GABA promotes weight loss and alleviates pain, but these studies did not resolve which signal mediates the effects. The goal of this study was to reveal the physiologic role of LHA-expressed Nts. We hypothesized that depleting Nts from the LHA of adult mice would promote weight gain and pain. To test this, we injected *Nts^{flox/flox}* mice in the LHA with either AAV-GFP (to generate Controls with intact LHA Nts expression) or AAV-Cre to deplete Nts expression from the LHA (referred to as Δ Nts mice). The Δ Nts mice gained more weight compared to Control mice and had altered feeding. Additionally, Δ Nts mice had increased hypersensitivity via the von Frey test compared to Controls, indicative of increased pain sensitivity. Since LHA Nts neurons release Nts to ventral tegmental area dopamine neurons that modulate feeding and pain, we hypothesized that Nts depletion might disrupt the dopamine system. Indeed, using the amphetamine-induced locomotor assay as a proxy of dopamine system function we found that Δ Nts mice had blunted amphetamine-induced locomotor response compared to Controls. Intriguingly, mice with diet-induced obesity have reduced Nts expression in the LHA along with blunted mesolimbic DA function and comorbid pain hypersensitivity, similar to the phenotype of Δ Nts mice. Together, these data suggest that loss of Nts in the LHA may contribute to the development of “gain and pain”, and hint that augmenting LHA Nts-mediated signaling may be useful to treat comorbid obesity and pain.

P140 **Rapid Fluctuations In Histamine Associated With Intake Of Nutritive And Non-Nutritive Solutions In Male Mice**

K. Linnea Volcko¹, Andrea Gresch², Barbara Benowitz³, Hamid Taghipourbibalan¹, Marije Visser¹, Garret D. Stuber³, Adam G. Gordon-Fennell³, Tommaso Patriarchi², James E. McCutcheon¹

¹UiT The Arctic University of Norway, Tromsø, Norway, ²University of Zurich, Zurich, Switzerland, ³University of Washington, Seattle, WA, United States

The neurotransmitter histamine is associated with control of appetite. While slow changes in histamine levels have been measured by microdialysis, to our knowledge, rapid changes in histamine release associated with behaviourally relevant events have not been demonstrated. Here, we used a novel fluorescent biosensor for histamine (HisLightG) to show rapid changes in histamine during consumption of nutritive and non-nutritive solutions. We confirmed selectivity of HisLightG by examining responses in HEK293T cells expressing HisLightG. Histamine application resulted in a large increase in fluorescence, which was not observed with other neurotransmitters. To measure histamine fluctuations *in vivo*, we used fibre photometry to record fluorescent responses in male C57BL/6N mice (n=12-15) and targeted paraventricular nucleus of the hypothalamus (PVH) or ventromedial hypothalamus (VMH). During consumption of nutritive (“Ensure”) or non-nutritive (sucralose) solutions, we observed consistent decreases in PVH at the start of lick bouts with a corresponding increase at the end of each bout. These responses were similar for both Ensure and sucralose and were not influenced by food restriction. No change in fluorescence was seen in VMH or in control mice expressing GRAB-DA in PVH. To demonstrate a behavioural effect of histamine manipulation, we trained food-restricted mice to lick for different concentrations of sucrose. Administration of the histamine precursor, L-histidine (500 mg/kg), led to a decreased licking rate, relative to saline. Together, these findings support the role of histamine release in appetite suppression and suggest that rapid fluctuations in histamine, rather than simply slow tonic changes, may be involved in the termination of distinct feeding bouts.

P141 **Neuronal Activation Patterns In Feeding Behavior: Exploring Amylin And Salmon Calcitonin With A Trap-Creert2 Mouse Model**

Kathrin von Bassewitz, Giulia Mazzini, Thomas A. Lutz, Christelle Le Foll
Institute of Veterinary Physiology, University of Zurich, Zurich, Switzerland

Gut hormones, in particular amylin and its analogues, have emerged as potential strategies to treat obesity due to their ability to influence feeding behavior, body weight, and energy expenditure by activating specific brain regions. One key target and entry point for their action is the area postrema (AP), which sends signals to other brain regions such as the nucleus of the solitary tract (NTS), the lateral parabrachial nucleus (LPBN), and the central amygdala (CeA). Building on our previous results suggesting that amylin and its analogue salmon calcitonin (sCT) only partly share the same neurocircuitry (amylin, but not sCT, promotes anorexia without inducing any aversive effects), we here employed a TRAP (Targeted Recombination in Active Populations) mouse model to examine neuronal activation patterns following amylin and sCT injections and investigate whether both peptides activate the exact same neurons. Initial injections of amylin or sCT in combination with 4-hydroxytamoxifen (4-OHT) facilitated the permanent labeling of activated neurons, producing a tdTomato fluorescence. No fluorescence was observed in mice injected with a stimulus but no 4-OHT. To assess the co-labelling, an immunohistochemical approach, using c-Fos as a marker, identified activated neurons after a second stimulation. Results indicate that amylin and sCT activate a comparable number of neurons among all analyzed brain regions (AP, NTS, LPBN, CeA). However, the number of neurons co-activated by both peptides was relatively low in all nuclei, with the highest percentage (10%) observed in the AP. Together, these findings highlight that although amylin and sCT are structurally and functionally similar, sCT seems distinct from amylin in the activation of neuronal pathways to mediate their anorectic effects.

P142 **Obesogenic Related Genes In The Female Hypothalamic Arcuate Nucleus Are Rescued By Exercise: A Potential Role Of Mir-211 Modulation**

Aron Weller¹, Kayla Rapps^{1,2}, Asaf Marco³, Hilla Pe'er-Nissan¹, Tatiana Kisoulik², Gabrielle Stemp¹, Gal Yadid¹, Noam Meiri²

¹Bar Ilan University, Ramat-Gan, Israel, ²The Volcani Center, Bet Dagan, Israel, ³The Hebrew University of Jerusalem, Rehovot, Israel

Obesity is a major public health concern that is associated with negative health outcomes. Exercise and dietary restriction are commonly recommended to prevent, or combat obesity. This study investigates how voluntary exercise mitigates abnormal gene expression in the hypothalamic arcuate nucleus (ARC) of diet-induced obese (DIO) rats. A transcriptomic approach assessed novel genes in the ARC that affect DIO by voluntary wheel running, and a combined approach of physiology, pharmacology, transcriptomic and bioinformatics analysis were used to evaluate the role of miR in the reversal

of obesity. Exercise curbed weight gain, fat mass, and restored ARC gene expression. As high-fat diet (HFD) consumption can cause dysregulation of satiety/hunger regulation mechanisms in the ARC, we outlined transcriptional clusters which depicted alterations in gene expression patterns via running, including inflammation and cellular structure genes. To uncover regulatory mechanisms governing gene expression in DIO attenuation, we explored the role of miR-211, as it has been implicated in systemic inflammation. The DIO overexpression of miR-211 was ameliorated by exercise, demonstrating its pivotal role in the regulation of inflammation in the ARC. Further, *in vivo* central administration of miR-211-mimic affected the expression of immunity and cell cycle related genes. By cross-referencing exercise-affected genes and miR-211-regulated genes, potential candidates for obesity reduction through exercise were identified. This research suggests that exercise may have a rescue effect on obesity through changes in gene expression that are mediated partially through miR-211.

P143 **Effects Of Maternal Metabolic Stress On Offspring Health And Peripheral Neurocircuit Development**

Rhonda Sin-Ling Chee^{1,2}, Sarah Xinwei Luo^{1,2}

¹Institute of Molecular and Cell Biology, Agency for Science, Technology and Research (A*STAR), Singapore, Singapore,

²Department of Physiology, Yong Loo Lin School of Medicine, National University of Singapore (NUS), Singapore, Singapore

Increasing evidence demonstrates that the maternal in-utero environment and early-life exposures influence health and vulnerability to disease later in life. While most have focused on the influence of the maternal metabolic environment on brain development of offspring resulting in dysfunctional neural development and behaviour disorders, little is known about its impact on peripheral nervous system development in offspring. We hypothesize that exposure to a maternal obesogenic diet induces alterations in peripheral nerve development in metabolic organs such as the liver, contributing to a predisposition for future metabolic disorders. Using three-dimensional immuno-imaging, we describe a general reduction in density of hepatic sympathetic innervation in these HFD-exposed pups. Ongoing works include investigating the role of Kupffer cells in neurite outgrowth during development, and RNA-sequencing of offspring liver samples. In all, this work will provide evidence for the need for early-life interventions for the prevention of long-lasting debilitating metabolic outcomes in offspring.

P144 **A Small Molecule Glp-1R Agonist Pf-06883366 Improves Glycemia, Reduces Food Intake, And Promotes Body Weight Loss In An Obese Humanized Glp-1R Mouse Model**

Ryan M. Esquejo¹, Zhenhong Li², Jeonifer Garren³, David R. Derksen⁴, Dong Yan¹, Nalissa Lynn Amar¹, Amit S. Kalgutkar², David A. Griffith², Kendra K. Bence¹, Jean-Philippe Fortin¹

¹Internal Medicine Research Unit, Pfizer Inc., Cambridge, MA, United States, ²Medicine Design, Pfizer Inc., Cambridge, MA, United States, ³Global Biometrics and Data Management, Pfizer Inc., Cambridge, MA, United States, ⁴Discovery Sciences, Pfizer Inc., Groton, CT, United States

Peptide-based glucagon-like peptide-1 receptor (GLP-1R) agonists are efficacious type 2 diabetes mellitus (T2DM) and obesity therapies that act by enhancing glucose-dependent insulin secretion and improving energy balance. Potent orally bioavailable small molecule GLP-1R agonists have recently been discovered and are actively being pursued as more convenient treatment options. Here, we evaluated the glycemic and anti-obesity effects of a small molecule GLP-1R agonist, PF-06883366, using a humanized GLP-1R (hGLP-1R) mouse model. To explore how different routes of administration may impact drug efficacy, PF-06883366 was delivered subcutaneously or orally at doses providing similar systemic exposures. In lean hGLP-1R mice, a single dose of PF-06883366 resulted in an improvement in glucose tolerance and a reduction in overnight food intake. In diet-induced obese (DIO) hGLP-1R mice, daily dosing with PF-06883366 for three weeks led to a dose-dependent reduction in cumulative food intake, body weight and fat mass that were associated with lower liver triglyceride, plasma lipids, and improved glucose tolerance. Quantitative pharmacokinetic-pharmacodynamic modeling supports that oral and subcutaneous administration of PF-06883366 produce similar beneficial effects on food consumption and body weight in obese mice when systemic exposures are comparable. Our study supports the therapeutic potential of emerging oral small molecule GLP-1R agonist therapies for the treatment of T2DM and obesity.

P145 **Morphological Diversity And Biophysical Properties Of Rat Epididymal White Adipocytes In Culture**

Maria Ortego-Dominguez^{1,2}, Rafael J. Montoro¹

¹Department of Medical Physiology and Biophysics. University of Seville, Seville, Spain, ²Department of Pharmacology, University of Michigan, Ann Arbor, MI, United States

Adipocytes participate in the metabolic regulation of the body through the storage of lipids and the release of special hormones, adipokines. In this work, we study the development of the morphological features of the cells, as well as some biophysical properties of white adipocytes in primary cultures. We classified these cells across time in culture into three different morphological types, M1, M2 and M3, according to the number of big lipid droplets in the cytoplasm. In spite of a huge increase in the number of cells across the time of study, the percentage of these three morphological types remained constant. This suggests that these cell types are distinct and not due to maturation from one stage to another. Next, we examined biophysical characteristics of these cell types using the patch-clamp technique in whole-cell configuration and voltage-clamp mode. For the passive properties, we noticed that membrane resistance and specific membrane resistance changed significantly over time in culture, but not capacitance. On the other hand, there were differences between the three morphological groups in the capacitance and specific membrane resistance, but not in the membrane resistance. Examination of active properties displayed variations in threshold, current and current density across days in culture. In regard to the morphological groups, we found differences in threshold and current amplitude, but not in current density. Finally, voltage and time dependent inactivation showed similar values across time and between morphology groups. The results from this work suggest three types of white adipocytes in primary culture, and some changes in the biophysical properties of the cells during the development of the culture.

P146 **Comparison Between The Effect Of A Novel Interview-Style Laboratory Stressor And The Trier Social Stress Test On Cortisol And Energy Intake In Young-Adult Females.**

Cecelia Redding¹, Brittany Campanella¹, Brent Howes¹, Lillyan Kingsbury¹, Tamari-Rose Love¹, Kavorn McKoy¹, A. Janet Tomiyama², Naomi J. McKay¹

¹SUNY Buffalo State, Buffalo, NY, United States, ²University of Southern California, Los Angeles, CA, United States

Cortisol reactivity in response to a stressor is associated with elevated energy intake. Cortisol, however, does not reliably elevate in response to many stressors used to test stress-induced energy intake. For example, the Trier Social Stress Test (TSST), which is a mock-job interview, is commonly used, but does not always stimulate a consistent elevation of cortisol. It is possible that the artificial nature of the task may dampen stress reactivity. Therefore, the current study tested two hypotheses. First, that a realistic interview would elevate cortisol more than the TSST, and second, that a realistic interview would stimulate higher energy intake compared to the TSST. Participants (n = 46 to date) were females 18-30 years old, and were randomly assigned to one of three test conditions, TSST, Interview, or No Stress. During the TSST, participants engaged in a mock job interview in front of three committee members. During the Interview condition, participants were informed that they were going to start their visit with an interview to determine if they were eligible to participate, which then proceeded similar to the TSST. Participants in the No-Stress condition sat quietly in the lab. A basket of snack foods was offered to half the participants before, and half immediately after, their test session and energy intake was measured. Salivary cortisol was measured throughout the visit. Preliminary results found a trend that the Interview condition stimulated a more robust elevation of cortisol. In addition, both stressors significantly suppressed energy intake compared to the No-Stress condition. This indicates that a more realistic stressor may more reliably stimulate salivary cortisol, but that this might not result in a different effect on energy intake.

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The Thermogenic Effect Of Fgf21 Signaling Is Mediated By Both Brown And Beige Adipose Tissue Activation

Redin A Spann, Md Shahjalal H Khan, Sora Q Kim, Diana A Albarado, Sun O Fernandez-Kim, Sangho Yu, Heike Muenzberg, Christopher D Morrison
Pennington Biomedical Research Center, Baton Rouge, LA, United States

Our lab and others have shown previously that the increase in energy expenditure (EE) and other metabolic benefits observed when dietary protein is restricted are mediated by FGF21 signaling to the brain and that this phenotype can be blocked by *Ucp1* deletion in adipose tissue. Both brown (BAT) and beige adipose tissue exhibit a robust increase in thermogenic genes, however, it has been unknown what pathways downstream of the brain are responsible for increased thermogenesis. To help answer this question we used a mouse model that lacks the thermoregulatory gene *Prdm16* only in white adipose tissue (WAT), rendering them unable to produce beige adipose tissue, while leaving intrascapular BAT intact. We placed these mice on isocaloric low protein (LP, 5% casein) and control (20% casein) diets for 3 weeks and found that animals on LP diet had less body weight (BW) gain and greater food intake as expected, but *Prdm16* deletion had no impact. Next, we placed animals on LP or control high-fat diets and measured glucose and insulin tolerance. Again, as expected animals on LP diet had improved glucose handling, but there was no difference between genotypes. To determine if BAT is responsible for LP-induced thermogenesis, we included a group of animals that received a sympathectomy to the BAT pads, effectively blocking their activation, in conjunction with *Prdm16* deletion. We measured EE with indirect calorimetry and found that while neither *Prdm16* knockout in WAT nor BAT sympathectomy alone were sufficient to block the increase in EE, their combination effectively blocked the effect of LP. These studies demonstrate that both depots of thermogenic fat contribute to increased EE with LP and can exert the effect alone, but future studies must determine how each tissue is activated and adapts.

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Vagotomy Associates With Decreased Risk Of Anxiety-Related Disorders In A Nationwide Retrospective Cohort.

Cornelia F Richter¹, Karolina P Skibicka^{2,3}, Urs Meyer¹, Sabine Rohrmann⁴, Jean-Philippe Krieger^{1,2}

¹Institute of Veterinary Pharmacology and Toxicology, University of Zurich-Vetsuisse, Zurich, Switzerland, ²Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden, ³Department of Nutritional Sciences, Pennsylvania State University, State College, Pennsylvania, PA, United States, ⁴Division of Chronic Disease Epidemiology, Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland

Lesions of the subdiaphragmatic vagus nerve, especially vagal sensory neurons, reduce anxiety-like behavior in rats. However, whether disrupted vagal communication impacts the risk to develop anxiety and anxiety-related disorders in humans has not been tested. Hence, we studied individuals who underwent vagotomy (selective and truncal), a surgical resection of the vagus nerve. A retrospective cohort approach was applied using nationwide data from the Swedish National Patient Registry within 1970-2020. We compared the risk to develop anxiety-related disorders (ICD10 F20-28) between vagotomized patients (n = 8,315) and controls matched for age, sex and history of peptic ulcer disease (n = 40,855). This association was analyzed with Cox proportional hazards models, including death as competing risk. 683 vagotomy cases and 3,479 controls with a post-operative anxiety-related disorder have been identified. Analyses showed a significantly decreased risk of anxiety-related disorders, for patients who underwent vagotomy, or selective vagotomy, compared to those who did not (HR overall: 0.79, [0.73, 0.86]; HR selective: 0.78, [0.71, 0.85]; HR truncal: 0.87, [0.71, 1.05]). Overall, our findings support the existing hypothesis that vagal neurons exert an anxiogenic tone and further suggest that their disruption slows the development of anxiety-related disorders in humans.

9:30 - 10:00 AM	Riverwalk A
Coffee Break	
10:30 - 12:10 PM	Ballroom I-II
PRESIDENTIAL SYMPOSIUM	

Chair(s): Scott Kanoski

10:30 **What We Know About The Relationship Between Neurodevelopment And Weight Gain In Adolescents: Insight From The Abcd Study.**

Shana Adise

Children's Hospital of Los Angeles, Los Angeles, CA, United States

While social, environmental, and genetic mechanisms may predispose some individuals to obesity, differences in brain structure and function may also create and induce such predispositions for obesogenic behaviors; numerous cross-sectional and longitudinal studies have shown strong associations between increased weight status and variation in the brain. However, the temporal mechanisms (e.g., cause vs. consequence) are unknown: That is, do underlying deficits in brain structure and function contribute to causing obesity, or does weight gain contribute to changes in the brain structure and its function? Here, I will discuss our approach to addressing this question, using data from a subset of youth enrolled in the Adolescent Brain Cognitive Development (ABCD) Study. We followed youth for two-years who at baseline (9/10-years-old), had a healthy weight, to understand the relationship between the natural progression of weight gain and neurodevelopment while disentangling effects of social determinants of health; neurodevelopment was assessed across several modalities (e.g., magnetic resonance imaging, behavioral assessments of executive function and cognition). The ABCD Study is large and diverse, thus providing a unique opportunity to investigate these relationships during a critical time in development for brain maturation and weight gain risk: adolescence. At large, findings show that underlying differences in brain structure and function, prior to unhealthy weight gain, relate to increases in body mass index over a two-year period in adolescence. However, two-years of weight gain may not be substantial enough to affect neurodevelopment, and continued collection and analysis of ABCD data will help parse the brain-to-obesity (or vice versa) pathway.

10:55 **The Role Of Endogenous Opioids In Motivation And Metabolism**

Daniel Castro

Washington University School of Medicine in St. Louis, Saint Louis, MO, United States

Since their discovery, exogenous and endogenous opioids have been shown to play a profound role in shaping motivation, affect, and reward. This is perhaps best captured by the current opioid epidemic in the United States, which claimed more than 100,000 lives from overdose last year. Opioids have a variety of important functions, including their effects on mesocorticolimbic circuits of reward (e.g., ventral tegmental area, nucleus accumbens). Here, opioids have been shown to influence both appetitive and aversive behaviors, particularly as it relates to food reward. Though important and foundational studies, comparatively little effort has been made to understand how opioids shape behaviors outside of canonical reward circuits, and indeed, outside of the brain. Recent work in our lab has sought to understand the role of opioids in non-canonical neural circuits of affect and motivation. Current efforts are centered on the opioid-rich dorsal raphe nucleus. Using iterative fluorescent in situ hybridization, selective CRISPR knockdown, and a wide array of behavioral assays, we have found that endogenous enkephalin and nociceptin opioid peptides in dorsal raphe nucleus appear to have complementary, albeit opposing, roles in aversive processing. Beyond the brain, we also explore how opioids can directly impact the hormonal and metabolic function of endocrine pancreas. Specifically, we show that mu opioid receptors can dramatically shape insulin and glucagon secretion, we well as overt ingestive patterns across the lifetime. Additionally, we have mapped the expression of opioids across endocrine pancreas cell types. Future work will evaluate how dorsal raphe opioid circuits engage downstream targets, and how opioids impact specific endocrine pancreas subpopulations.

11:20 **Noradrenergic Modulation Of Cortical Taste Processing**

Will Fan¹, Natale Sciolino¹

¹Department of Physiology and Neurobiology, University of Connecticut, STORRS, CT, United States, ²Department of Physiology and Neurobiology, University of Connecticut, STORRS, CT, United States

Taste plays a fundamental role in our consummatory decisions. The primary taste cortex (GC) constructs holistic food perceptions by integrating taste with multisensory information, bodily states, and experience. The GC receives a prominent neuromodulatory input from noradrenergic neurons in the locus coeruleus (LC), yet its effects on taste processing remain unknown. Using pathway-specific optogenetics, we found that stimulation of the LC-GC pathway significantly heightens the preference for a novel, palatable tastant (saccharine) and facilitates appetitive taste learning. To determine the impact of LC input on GC encoding, we used a miniature microscope system to activate LC axons while monitoring either the spontaneous or taste-evoked calcium activity in individual GC neurons. Our results demonstrate that activation of the LC-GC pathway exerts divergent effects on the spontaneous activity of GC taste responsive neurons. Given that LC neurons are transiently activated during anticipation of gustatory rewards, we next sought to determine if brief activation of the LC-GC pathway would influence GC taste-evoked responses. We found that brief activation of LC axons during sucrose approach predominantly enhanced GC excitatory response to sucrose consumption. Further, we found that activating LC projection broadens the tuning of GC neurons to four basic tastes (sweet, salty, sour, bitter), highlighting LC's capacity to restructure cortical taste representation. In conclusion, our findings uncover a novel role for LC neurons in modulating cortical taste encoding, as well as taste perception and learning.

11:45 **Wild, West, Wireless: Changing Rural Teenage Girls' Eating Behaviors Through Mobile Phones**

Grace E. Shearrer

University of Wyoming, Laramie, WY, United States

Mobile phone applications (apps) are an attractive intervention method to reach rural adolescents. We have adapted Dr. Hedy Kober's regulation of craving training (ROC-T) intervention into a value aligned mobile phone app for rural teenage girls to improve consumption of fruits and vegetables. Rural populations have a 16% higher prevalence of type 2 diabetes (T2D) compared to their suburban and urban counterparts. Improving diet, particularly increasing fruit and vegetable consumption, is a protective factor against developing T2D. However, only 13.1% of Wyoming girls eat vegetables 3 times a day. Female adolescents tend to eat less fruits and vegetables compared to males, and intake decreases with age. This is particularly concerning given T2D is more aggressive in adolescents and is 60% more prevalent in adolescent girls compared to boys. Craving unhealthy food is a noted barrier to healthy eating in adolescents. Personalized interventions, such as the ROC-T, can reduce cravings. ROC-T improves food choice through autonomous self-control and changing the value of the craved food. An effective approach to engage with adolescents is to use a value aligned intervention to relate food choice to values adolescents care about and build personal autonomy. The mobile regulation of craving training (mROC-Teens) combines the existing ROC-T intervention with value aligned messaging in an app to reach and engage with rural girls. In addition to the app, we have designed a mobile health lab from a recreational vehicle (RV) trailer to perform baseline and follow up diabetes testing using point of care hemoglobin A1c and glucose testing. The presentation will give an overview of the development of the app and mobile testing lab, rollout of the intervention, and future directions.

12:15 - 1:45 PM	On Own
Lunch	
1:45 - 3:30 PM	Ballroom I-II
Oral Session 1: What's My Motivation?	

Chair(s): Jamie Roitman

1:45

Taste Evoked Dopamine And Norepinephrine Track Liking In The Human Amygdala

Seth R. Batten¹, Beniamino Hadj-Amar², Monica L. Ahrens³, Mary E. Oster¹, Alec Hartle⁴, Leonardo S. Barbosa¹, Terry Lohrenz¹, Jason P. White¹, Mark R. Witcher⁵, Marina Vannucci², P. Read Montague^{1,6,7}, W. Matthew Howe⁴, Alexandra G. DiFeliceantonio^{1,8}

¹Fralin Biomedical Research Institute, Virginia Tech, Roanoke, VA, United States, ²Department of Statistics, Rice University, Houston, TX, United States, ³Center for Biostatistics and Health Data Science, Department of Statistics, Blacksburg, VA, United States, ⁴School of Neuroscience, Virginia Tech, Blacksburg, VA, United States, ⁵Division of Neurosurgery, Virginia Tech Carilion School of Medicine, Roanoke, VA, United States, ⁶Department of Physics, Virginia Tech, Blacksburg, VA, United States, ⁷Wellcome Centre for Human Neuroimaging, University College London, London, United Kingdom, ⁸Department of Human Nutrition, Foods, and Exercise, Virginia Tech, Blacksburg, VA, United States

Attributing value to taste depends on the integration of central gustatory signals with reward-related computations. There is strong evidence that the amygdala is a site where such integration occurs. For example, the amygdala has strong reciprocal connections between primary gustatory cortex, gustatory thalamus, and brainstem. Functional evidence suggests that topographically distinct regions of the gustatory cortex that encode sweet and bitter sensation in rodents project to the amygdala. Further, human fMRI studies reliably report amygdala activation to taste stimuli, and lesions to the amygdala impair preferences for food cues in humans. While electrophysiological recordings from human amygdala reveal food-specific valuation encoding in a preference task, little is known about the neurochemical dynamics in this region. Here we used a novel technology that allows neurochemical measurements on depth electrodes used during standard of care in epilepsy monitoring to measure dopamine (DA) and norepinephrine (NE) in the amygdala while people ($n = 3$) consumed beverages with varying amounts of fat and sugar. We observed that DA increased and NE decreased following consumption of the high fat beverage ($X^2_{(6)} = 202.7, p < 0.0001$). Following consumption of the low-fat beverage, DA was lower than NE ($X^2_{(6)} = 26.71, p = 0.0003$). Each participant rated each beverage on the labeled hedonic scale. Further analysis revealed that DA increases were associated with drinks with high liking ratings, while NE increases were associated with drinks with low liking ratings ($t(68) = -2.41, p = 0.018$). Collectively, these findings demonstrate our capacity to monitor sub-second DA and NE signaling in the human amygdala during food intake and represent a first-of-their-kind test of the translatability of key findings from animal models.

2:00

Cue-Triggered "Wanting" Is Increased In Participants With Obesity Compared To Healthy-Weight Participants

Geraldine Coppin^{1,2,3}, Kinga Igloi^{1,3,4}, Eva R Pool^{1,2}, David Munoz-Tord^{1,2,3}, Loic Locatelli⁵, Amal Achaibou^{1,3}, Asli Erdemli^{1,2}, Laura Leon-Perez^{1,2}, Lavinia Wuensch^{1,2}, Donato Cereghetti¹, Alain Golay⁵, David Sander^{1,2}, Zoltan Pataky⁵

¹Swiss Center for Affective Sciences, University of Geneva, Geneva, Switzerland, ²Department of Psychology, University of Geneva, Geneva, Switzerland, ³Department of Psychology, UniDistance Suisse, Brig, Switzerland, ⁴Department of Neuroscience, Faculty of Medicine, University of Geneva, Geneva, Switzerland, ⁵Department of Medicine, University of Geneva, Geneva, Switzerland

Food reward is not a unitary concept. While "liking" refers to the hedonic pleasure during food consumption, "wanting" refers to the motivation to obtain a reward. Studies comparing these two sub-components in healthy-weight individuals (HW) and participants with obesity (OB) have brought mixed evidence. Here we compared their behavioral and neural correlates. Participants came in the laboratory after overnight fasting. They reported their liking while consuming a milkshake and a tasteless solution. Participants also completed an analog of a Pavlovian-Instrumental Transfer test to measure "wanting". They first learned to associate a neutral geometric figure (CS+) to a food reward and an instrumental action to the reception of this reward. We then measured the influence of the Pavlovian stimuli associated to food reward on the effort mobilized. The solutions were administered inside the scanner with a MRI-compatible gustometer. 25 age and gender matched HW (BMI = 22.37±1.77) and 57 OB (BMI = 35.54±3.15) were tested. Our behavioral results did not show any significant difference in liking between HW and OB. However for wanting there was a significant GroupXCondition interaction effect ($p=0.049$), OB participants showing increased wanting in the CS+ compared to the CS- condition ($p=0.017$). When contrasting neural responses to the CS+ vs. CS-, we found increased prefrontal activation in OB, and increased cerebellar activation (in particular of lobe VIII and Crus II regions) in HW. We could speculate that OB exert more control in these high-calorie food-related tasks explaining increased prefrontal activation, whereas HW rely more on the posterior cerebellum as part of a self-related emotional processing network.

2:15

Motivational State-Dependent Control Of Feeding By An Extended Amygdala To Lateral Hypothalamic Area Pathway

Kuldeep Shrivastava¹, Vikshar Athreya¹, Mark A. Rossi^{1,2,3}

¹Child Health Institute of New Jersey, New Brunswick, NJ, United States, ²Department of Psychiatry, Robert Wood Johnson Medical School, New Brunswick, NJ, United States, ³Rutgers University Brain Health Institute, Piscataway, NJ, United States

The lateral hypothalamic area (LHA) regulates motivated behavior, including feeding. It exerts control over behavior via distinct cell types and diverse synaptic connectivity. Glutamatergic LHA neurons suppress food intake, and their activity is modified by fasting, feeding hormones, and diet-induced obesity. However, the circuit mechanisms by which motivational state guides LHA glutamate neuron activity are unknown. A major source of synaptic input to these neurons is from GABAergic neurons of the bed nucleus of the stria terminalis (BNST). Manipulations of this pathway influence feeding and reward. We therefore *hypothesized* that the BNST to LHA pathway contributes to changes in LHA glutamate neuron activity that adjust food seeking to meet energy demands. Using optogenetic perturbations in mice (n>10/group), we show that the function of the BNST to LHA pathway depends on motivational state: feeding induced by BNST to LHA stimulation is potentiated by fasting and attenuated by over-feeding. Ex vivo electrophysiological recordings from LHA glutamatergic neurons receiving monosynaptic BNST input (n=13 cells/group) confirm that this is caused by tuning synaptic strength. By combining in vivo multiphoton imaging of LHA neurons with simultaneous optogenetic activation of BNST inputs, we demonstrate that LHA glutamate neurons exhibit prolonged inhibition in response to BNST axon activation. In agreement with our behavioral results, LHA glutamate neuron inhibition induced by BNST stimulation is enhanced by fasting and attenuated by over-feeding (n=7 mice; >50 cells/condition). Together, these results suggest one way by which the activity of lateral hypothalamic glutamate neurons is modified by presynaptic input to orchestrate feeding behavior according to energy needs.

2:30

Hippocampus Dopamine Signaling Is Modulated By Eating And Promotes Meal-Related Memories Via Dopamine Type 2 Receptors

Alexander G Bashaw^{1,2}, Lea Decarie-Spain¹, Logan Tierno-Lauer¹, Alicia Kao¹, Ryan Wisniewski¹, Scott E Kanoski^{1,2}

¹Human and Evolutionary Biology Section, Department of Biological Sciences, Dornsife College of Letters, Arts and Sciences, University of Southern California, Los Angeles, CA, United States, ²Neuroscience Graduate Program, University of Southern California, Los Angeles, CA, United States

In both humans and experimental rodent models, disruption of meal-related episodic memories leads to excessive consumption during subsequent eating episodes. The Hippocampus (HPC), a brain region known for its role in learning and memory, is associated with food intake control via its mediation of meal-related episodic memory. The neurochemical mechanisms through which the HPC encodes meal-related memories, however, are poorly understood. Dopamine (DA) is a neurotransmitter critically involved in food-related reinforcement learning. While DA signaling in the striatum has been widely investigated, far less is known about DA function in the HPC. Human PET imaging studies find elevated DA in the HPC after subjects consume a milkshake, and in mice, silencing or activating DA type 2 receptor (D2R)-expressing HPC neurons bidirectionally affects food intake. Building off these findings, here we directly evaluated the role of HPC DA receptor (D1R, D2R) signaling in meal-related memory in rats using a behavioral neuropharmacological approach. Results reveal that HPC D2R but not D1R activation reduced short-term food intake, and that D2R but not D1R blockade impaired memory for meal location. To investigate the signaling dynamics of HPC DA release surrounding meal consumption, we used fiber photometry to detect the changes in HPC DA signaling (via D2R-based fluorescent sensors) before, during, and after meal consumption in food-restricted rats. We found that DA binding was dynamically reduced during the first eating bout of the meal but was significantly elevated in the post-meal relative to the pre-meal state. Collective results identify HPC DA-D2R signaling as a candidate neurochemical mechanism through which nutrient consumption promotes meal-related episodic memory formation.

2:45

Food Reinforcement Is Positively Associated With Eating In The Absence Of Hunger Among Children With Low Satiety Responsiveness (New Investigator Travel Awardee)

Kyle Hallisky¹, Nicholas V. Neuwald¹, Stephen J. Wilson¹, Travis Masterson¹, Emma J. Rose¹, Frank G. Hillary¹, Amanda Bruce², Hugh Garavan³, Seung-Lark Lim⁴, Kathleen L. Keller¹

¹The Pennsylvania State University, University Park, PA, United States, ²The University of Kansas Medical Center, Kansas City, KS, United States, ³The University of Vermont, Burlington, VT, United States, ⁴University of Missouri-Kansas City, Kansas City, MO, United States

The reinforcing value (RV) of food (motivation to work for food), is associated with obesity in children. However, the extent to which the RV predicts children's intake under different conditions (e.g. meals consumed fasted, snacks in the absence of hunger-EAH) is unknown. We tested the hypotheses that RV would be positively associated with intake at both meals and EAH, and that appetitive traits such as satiety responsiveness (SR) would moderate this association. As part of an ongoing 5-visit, longitudinal study, 61 children (7-9 years <95th BMI%) completed a relative RV task (Visit 1) to assess willingness to work for candy and toys. P_{max} (number of reward schedules completed) was measured for each reinforcer. Prior to the task children consumed a meal to fullness. On visit 3 and 4, 20 min after a meal, EAH was measured as children's energy intake from 10 min of free access to 9 sweet and savory snacks. SR was assessed from parent report using the Children's Eating Behavior Questionnaire. Children worked equally for both candy and toys (p=.86). Linear regressions (adjusted for age, sex, BMI%, income, liking, fullness) showed a positive relationship between both candy (p=.03) and toy P_{max} (p=.02) with energy intake at the pre-task meal. However, P_{max} was not associated with meal energy intake from visits 3 and 4. SR moderated the association between two measures of reinforcement and EAH (ps<.05). In those with low SR, RV and EAH were positively associated (p<.05). No association was seen in those with high SR. This demonstrates that the willingness to work for food is associated with greater energy intake during a meal and EAH (among low-SR children). Interventions for promoting SR may help mitigate the effects of high food reinforcement on non-hunger-related intake.

Dopamine Neurons In The Zona Incerta And Their Distinct Role In Food Seeking Motivation

Qiyang Ye, Jeremiah Nunez, Xiaobing Zhang
Florida State University, Tallahassee, FL, United States

The zona incerta (ZI) is a key region in the subthalamus, known for its involvement in sensory processing, motor control, and feeding control. While predominantly comprising GABAergic neurons, the ZI also contains a distinct population of tyrosine hydroxylase (TH) neurons. The specific roles of these dopamine (DA) neurons, particularly in the context of motivational aspects of food intake, are not fully understood. Our study examines the ZI DA neurons' role, less studied compared to the dopamine system in the ventral tegmental area (VTA), in hunger-induced food-seeking. We demonstrate that these neurons, along with their projections to the paraventricular thalamus (PVT), exhibit dynamic activity patterns that are closely associated with feeding motivation. We have revealed that the activation of ZI DA neurons increases meal frequency rather than the total amount consumed, delineating their function from that of ZI GABA neurons, which significantly increase overall food intake upon activation, contributing to binge-eating-like behaviors. Subsequent operant conditioning tests illustrate that activation of these DA neurons significantly enhances food-seeking behaviors and is instrumental in the development of contextual memories linked to food rewards, highlighting their role in encoding motivational vigor for food consumption. Through calcium imaging, we have discerned that ZI DA neurons respond distinctly to the approach and consumption of food in comparison to ZI GABA neurons, suggesting specialized roles within the feeding control. Our findings add a new dimension to our understanding of the neural circuits that govern motivation and feeding behavior, with potential implications for addressing disorders related to abnormal eating behaviors.

Fasting Satiety Liver/Foregut Hormone Leptin Negatively Correlates With High Energy Versus Low Energy Food Cue Reactivity In Adults With Obesity

Mimoza Emini¹, Raghav Bhargava¹, Marcela Rodriguez Flores¹, Navpreet Chhina¹, Ghadah Aldubaikhi¹, Moaz Al Lababidi¹, Lilliam Flores¹, Aruchuna Ruban², Christina G Precht³, Julian P Teare², Anthony P Goldstone¹

¹PsychoNeuroEndocrinology Research Group, Division of Psychiatry, Department of Brain Sciences, Imperial College London, London, United Kingdom, ²Department of Surgery and Cancer, Imperial College London, London, United Kingdom, ³Clinical Trials Unit, Department of Public Health, Imperial College London, London, United Kingdom

Background: LEAP2 is a gut hormone acting as an inverse agonist at the acyl ghrelin receptor (GHSR). In rodents, LEAP2 attenuates exogenous AG-induced and spontaneous food intake. In humans without obesity, exogenous LEAP2 decreases ad libitum food intake, and post-prandial increases in plasma LEAP2 correlate with post-prandial decreases in appetite and food cue reactivity. However, any inhibitory influence of LEAP2 on food cue reactivity, and potential preferential effects on high/low energy (HE/LE) foods, in obesity is unknown. **Methods:** Overnight fasting plasma LEAP2 was assayed in n=46 adults with obesity (31-64 years, 51% female, 76% T2DM, BMI 30-56 kg/m²) completing food picture evaluation fMRI task for HE and LE foods, fasting appetite visual analogue scale ratings, post-MRI *ad libitum* food intake (as % estimated resting energy expenditure), motivation for sweets in progressive ratio task (PRT) 2 hours later. **Results:** Plasma LEAP2 negatively correlated with BOLD signal averaged across all fROIs (P=0.030, nucleus accumbens (NAcc), caudate, putamen, amygdala, ant. insula, OFC), and in NAcc alone (P=0.019) to HE vs. LE foods. This was driven by positive correlations with BOLD signal to LE foods (P=0.028-0.030), rather than negative correlations to HE foods (P=0.90-0.94). Similar results were seen when including BMI or fasting plasma glucose as covariates. Plasma LEAP2 tended to correlate negatively with appeal rating for HE vs. LE foods (P=0.01), but did not correlate with appetite, ad libitum energy intake, nor PRT breakpoint (P=0.72-0.99). **Conclusion:** These relationships of fasting plasma LEAP2 with food cue reactivity, provides novel evidence supporting a role for LEAP2 inhibition of GHSR signalling in attenuating human (over)eating behaviour in obesity.

Oral Session 2: KIDding Around About Ingestive Behaviors

Chair(s): Lex Kravitz

1:45

Behavioral Inhibition Is Positively Associated With Eating In The Absence Of Hunger Among Children With Lower Satiety Responsiveness

Rhea Sarma, Alaina L Pearce, Kathleen L Keller

The Pennsylvania State University, University Park, PA, United States

The behavioral approach (BAS) and behavioral inhibition system (BIS) are two biobehavioral system that impact reward (BAS) and punishment (BIS) sensitivity. While greater behavioral approach is associated with greater food intake, the link between BIS and eating behavior is unclear. We hypothesized children with high BIS may be more sensitive to parental rules about snacking; thus, higher BIS would be associated with reduced eating in the absence of hunger (EAH) paradigm. We also tested whether satiety responsiveness (SR) moderated this relationship. 158 children (7-9 years, <90th BMI%) participated in one of two multi-visit longitudinal cohort studies. After consuming a standardized meal to fullness, they had free access to 9 energy-dense (>3.9 kcal/g) sweet and savory snacks for 10 min. EAH was calculated as children's energy intake from the 9 foods. Parents completed the Children's Eating Behavior Questionnaire and the BIS/BAS to assess SR and BIS, respectively. Adjusting for age, sex, BMI z-score, risk for obesity (determined from maternal BMI) and study, BIS was positively associated with EAH ($p = .006$). Moderation analysis revealed an interaction between SR and BIS on EAH ($p = .038$). Specifically, for children with lower SR, BIS was positively associated with EAH ($p = .003$), while no relationship was found in children with higher SR. Contrary to our hypothesis, BIS was positively associated with EAH among children who were less responsive to satiety cues. The findings provide initial evidence for an association between sensitivity to punishment and hedonic eating in children with lower SR, however, replication in a more diverse cohort of children is needed.

2:00

Effects Of Maternal Obesity On Leptin Signaling During Development In The Dorsal Motor Nucleus Of The Vagus

Eric T. Winzenried, Suzanne M. Appleyard

Washington State University, Pullman, WA, United States

Maternal obesity (MO) is associated with an increased risk of childhood obesity and development of type II diabetes. One factor thought to be impacted by MO is leptin signaling in offspring. Leptin is important for the development of circuits involved in the control of food intake and glucose regulation. The dorsal motor nucleus of the vagus (DMNV) is composed primarily of cholinergic motor neurons that project to the periphery, including the pancreas and GI. Leptin has been shown to effect DMNV neurons; however, how these effects change during development and the consequences of MO are not known. To investigate this, we performed whole-cell voltage clamp electrophysiological recordings in DMNV neurons of both male and female mice at post-natal day (PND) 10, 21, 35, 50, and 90. We found that leptin has broad effects on DMNV neurons throughout development including increasing and decreasing spontaneous excitatory post-synaptic current (sEPSC) frequency and inducing both inward (excitatory) and outward (inhibitory) currents. To examine the impact of MO, female C57BL/6J mice were fed a high-fat high-sugar diet, or control chow, for 8 weeks to induce obesity and then paired with non-obese males. MO appears to shift the effects of leptin to be more excitatory by increasing the proportion of cells that have an increase in sEPSC frequency and inward currents, particularly around PND35-50. Interestingly, MO also caused an increase in basal sEPSC frequency in DMNV neurons at this developmental stage. Taken together with previous research, it is possible that these changes induced by MO could contribute to its long-term consequences on body weight and glucose regulation.

2:15

Exposure To Ultra-Processed Foods Alters Brain Response To Milkshake In Adolescents And Young AdultsEmma H. Leslie^{1,2}, Maria Rego³, Wenjing Yu², Monica Ahrens⁵, Alexandra L. Hanlon⁵, Valisa E Hedrick³, Kevin P. Davy³, Benjamin Katz⁶, Brenda Davy³, Alexandra G. DiFeliceantonio^{2,3}

¹Graduate Program in Translational Biology, Medicine, and Health, Virginia Tech, Blacksburg, VA, United States, ²Fralin Biomedical Research Institute, Virginia Tech, Roanoke, VA, United States, ³Department of Human Nutrition, Foods, and Exercise, Virginia Tech, Blacksburg, VA, United States, ⁴Department of Biology, Virginia Tech, Blacksburg, VA, United States, ⁵Center for Biostatistics and Health Data Science, Virginia Tech, Roanoke, VA, United States, ⁶Department of Human Development and Family Science, Virginia Tech, Blacksburg, VA, United States

Ultra-Processed Food (UPF) are commercially processed foods that comprise over half the average American's diet (58% total energy); consumption is linked with diabetes and all-cause mortality. The only randomized controlled trial (RCT) exploring effects of UPF exposure reports higher *ad libitum* energy intake and weight gain in adults. Despite many rodent studies demonstrating diet-brain interactions, the impact of UPF consumption on brain reward response has not been examined in humans. Further, young adults are in a critical stage for developing food choices and have the poorest diet quality (68% total energy UPF). In our ongoing cross-over RCT, 32 young adults (aged 18-25) undergo a diet high in UPF (81% kcal UPF) and a nonUPF (0% kcal UPF) diet for 2 weeks each. Diets are eucaloric and matched in macro- and micro-nutrient content. Brain reward response is measured by exposing participants to an UPF milkshake predicted by a cue during concomitant fMRI before and after each diet period. A tasteless solution is used as a control stimulus and is predicted by a cue. Here, we report preliminary analyses on 11 participants. We observe an interaction effect in the caudate, with increased activity in response to milkshake (minus tasteless) cue post-UPF diet and decreased post-nonUPF diet [-8.14 ± 2.1 , $p_{FWE} = 0.032$, $T = 4.63$, $k = 51$, *a priori ROI*, SVC). Additionally, a whole brain corrected analysis shows an interaction effect in the hippocampus, with increased activity in response to milkshake (minus tasteless) delivery post-UPF diet and decreased post-nonUPF diet [30.14 ± 16.1 , $p < 0.001$ uncorr, $k = 67$]. Our results provide preliminary evidence that brain response to UPF milkshake and associated cues is altered after exposure to a high UPF diet.

Advanced Glycation End Products And The Gut Microbiome Underscore Memory Impairments Due To Early Life Consumption Of A "Processed" Diet In Rats

Anna M.R. Hayes¹, Alicia E. Kao¹, Natalie Tanios¹, Arun Ahuja¹, Isabella H. Gianatiempo¹, Molly E. Klug¹, Linda Tsan^{1,2}, Shan Sun³, Anthony A. Fodor³, Melinda T. Coughlan^{4,5}, Scott E. Kanoski^{1,2}

¹Department of Biological Sciences, Human and Evolutionary Biology Section, University of Southern California, Los Angeles, CA, United States, ²Neuroscience Graduate Program, University of Southern California, Los Angeles, CA, United States, ³Department of Bioinformatics and Genomics, the University of North Carolina at Charlotte, Charlotte, NC, United States, ⁴Department of Diabetes, Central Clinical School, Alfred Medical Research and Education Precinct, Monash University, Melbourne, Australia, ⁵Baker Heart and Diabetes Institute, Melbourne, Australia

Recent evidence indicates that "ultra-processed" foods constitute ~65% of total energy intake among children in the US. However, little is understood about the neurocognitive impacts of excessive processed food consumption during early life. Dry heat treatment is a common food processing step, which can induce the chemical Maillard reaction and lead to foods high in advanced glycation end products (AGEs). Here we evaluated the effects of consuming a heat-treated AGE-rich diet during early life on hippocampal (HPC)-dependent memory function and gut bacterial composition. Rats received an otherwise healthy AGE-rich diet (AGE rats; AIN-93G diet heated at 160°C for 60min) or a non-AGE-rich diet (CTL rats; AIN-93G diet without heat treatment) during adolescence (postnatal days [PN] 26-60). Half of the rats per diet group received a drug that disrupts AGEs (alagebrium, 1mg/kg/day) in drinking water (CTL+ALA, AGE+ALA) and the other half received drinking water alone (CTL+H₂O, AGE+H₂O). Results from behavioral assessments conducted during adulthood revealed that AGE+H₂O rats exhibited HPC-dependent contextual episodic memory impairments (novel object in context procedure) relative to AGE+ALA, CTL+H₂O, and CTL+ALA rats, indicating that dietary AGEs underlie the memory deficits. Gut microbial analyses revealed decreased abundance of the taxon *Lactococcus* associated with the AGE-rich diet. These changes appear to have a causal role in the memory impairments, as replenishing *Lactococcus lactis* (10⁹ colony forming units/day) via oral gavage administration from PN 26-40 during exposure to the heat-treated diet rescued the AGE-induced memory impairments. Collective findings reveal a connection between early life dietary AGEs, the microbial taxon *Lactococcus*, and impaired memory function.

Child And Parent Perceptions Of Alternative Proteins In Singapore

Aimee E. Pink^{1,2}, Siti Amelia Juraimi¹, Arunika Pillay², Nandini Anant¹, Yin Zhien Tan³, Florence Sheen⁴, Anna Fogel², Benjamin P. C. Smith⁵, Mary F-F. Chong³

¹Institute of High Performance Computing (IHPC), , Agency for Science, Technology and Research (A*STAR), Singapore, Singapore, ²Singapore Institute for Clinical Sciences (SICS), Agency for Science, Technology, and Research (A*STAR), Singapore, Singapore, ³Saw Swee Hock School of Public Health, National University of Singapore (NUS), Singapore, Singapore, ⁴School of Sport, Exercise and Health Sciences, National Centre for Sport and Exercise Medicine, Loughborough University, Loughborough, United Kingdom, ⁵Monell Chemical Senses Center, Philadelphia, PA, United States

Singapore aims to address its food security concerns by locally producing 30% of its nutritional needs by 2030. Increasing consumption of alternative proteins will help achieve this target. To date, research predominantly focuses on Western adults and neglects perceptions of non-Western countries, with even less research on children available. We conducted a qualitative study to understand children and parents' perceptions of alternative proteins (plant-based, cultivated meat, and insect proteins) and identify facilitators and barriers to consuming them within Singapore. Child (9-15 years) and parent (38-55 years) pairs (*N*=19) participated in focus group discussions with a semi-structured topic guide. Using reflexive thematic analysis, six themes were identified inductively including evaluation of product attributes, psychological factors, and parent-child influences, as examples. Next, with a deductive approach, sub-themes were sorted into facilitators and barriers for consumption of alternative proteins within the Capability, Opportunity, Motivation, and Behaviour (COM-B) model. Examples include a lack of cooking skills (barrier within Capability for plant-based meat) and a preference for sensory similarities to traditional meat (facilitator and barrier within Motivation for plant-based and cultivated meat). This qualitative study informs, and is complemented by, a quantitative study which aims to test the predictive ability of the COM-B model on child and parent consumption of alternative proteins in Singapore (targeted recruitment of *N*=600 parent-child pairs). By understanding perceptions of alternative proteins among children, who are our future consumers, and their parents allows us to develop interventions to increase acceptance and consumption.

Maternal Western Diet Reduces The Density Of Glucagon-Like Peptide 1 (Glp1) Axonal Inputs To The Thalamus And Hypothalamus In Rat Offspring

Abigail B Randolph, Linda Rinaman
Florida State University, Tallahassee, FL, United States

Rat offspring born to dams that consumed a diet high in fat and sugar (e.g., Western diet; WD) during pregnancy and lactation display an increased intake of palatable foods and changes in other reward-related behaviors. Normally, these outcomes are suppressed by central GLP1 signaling pathways. However, it is unknown whether maternal WD alters central GLP1 signaling in offspring. To evaluate this, we used a newly developed Gcg-Cre/*tdTomato* reporter rat model in which red fluorescent protein (RFP) is expressed in GLP1 neurons and their axonal projections [PMID: 36368622]. Dams were maintained on chow (controls) or were introduced to WD 3 days before mating and were maintained on the same diet through gestation and lactation. All offspring were weaned onto chow at postnatal day 21 (P21), when WD-reared offspring display significantly higher body weight and fat. At P14 and P60, the density of RFP-labeled GLP1 axons was quantified in feeding-related brain regions, including paraventricular nucleus of thalamus and hypothalamus (PVT, PVH), lateral hypothalamus (LHA), and dorsomedial hypothalamus (DMH). At P14, striking reductions in GLP1 axon density were observed in PVT, PVH, LHA, and DMH, with persistent effects remaining into early adulthood (P60). Thus, gestational and lactational exposure of offspring to maternal WD impacts the early development and later density of GLP1 axonal inputs to diencephalic regions, even in young adult offspring maintained exclusively on chow after weaning. Blunted central GLP1

signaling could have wide-reaching effects on offspring metabolism and behavior. These novel data provide valuable insight into the complex interplay between maternal nutrition and the development of neural circuits involved in metabolism and ingestive behavior.

3:30 - 4:15 PM	Riverwalk A
Coffee Break & Exhibits	
4:15 - 5:55 PM	Ballroom III
Symposium 1: Central Estrogen Signaling and Feeding Control	

Chair(s): Stephanie Kullman

4:15 **Effects Of The Menstrual Cycle Phase On Brain Response To Insulin And Food Cues**

Stephanie Kullmann

Institute for Diabetes Research and Metabolic Diseases of the Helmholtz Center Munich at the University of Tuebingen, Tuebingen, Germany

Menstrual cycle has a strong impact on food intake; however, underlying mechanisms are not clear. One well-known regulator of eating behaviour and metabolism is insulin action in the brain. In my talk I will address the impact of the menstrual cycle on the brain's responses to visual food cues and intranasal insulin using functional magnetic resonance imaging. I will show recent findings on how reduced hypothalamic insulin responsiveness might contribute to whole-body insulin resistance in the luteal phase in premenopausal women. Moreover, in the luteal phase of the menstrual cycle, intranasal insulin fails to influence hippocampal and striatal functional connectivity, while visual food cues evoke stronger reactivity in these brain regions. These responses are linked to higher estradiol and progesterone levels, pointing towards a role of sex hormones in neuroendocrine regulation of eating behaviour.

4:40 **Crucial Role Of Brain Aromatase In Feeding Behavior And Metabolic Homeostasis Control.**

Karolina Skibicka^{1,2,3}

¹Department of Nutritional Sciences, Pennsylvania State University, University Park, PA, United States, ²Huck Institutes, Pennsylvania State University, University Park, PA, United States, ³Institute for Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden

Aromatase is the sole enzyme responsible for converting androgens into estradiols. Estradiol orchestrates feeding behavior and metabolism; we and others found that it reduces ingestive and motivated behavior, increases energy expenditure, and interacts with gut-brain hormones like glucagon-like peptide 1 and ghrelin, by acting on estradiol CNS receptors. It is generally assumed that the estradiol supply for these receptors comes primarily from the gonads. However, in humans and rodents, neurons in discrete brain regions densely express aromatase. The role of brain aromatase and locally *de novo* (brain)-derived estradiols in energy balance control remain poorly understood. We found that pharmacological blockade of whole brain aromatase with letrozole, a clinically utilized aromatase inhibitor, increases body weight and food intake in female, but not male, rats. This suggests that brain synthesized estradiols have a key role in food intake and body weight control. We next set out to find the brain region with the highest expression of aromatase. We identified a dense population of aromatase-expressing neurons in the amygdala of male and female rats. Using a novel virogenetic approach to selectively target the amygdala aromatase we determined the role of amygdala aromatase in energy balance and food motivated behavior, under baseline and obesogenic diet conditions, in male and female rats. Collectively our results reveal a crucial role of amygdala-synthesized estradiols in maintenance of energy balance during metabolic health and disease. They may be translationally relevant, as aromatase inhibitors are in clinical use and a very recent study found reduced brain aromatase activity in obese patients.

5:05 **Time Restricted Eating And Female Sex Hormones**

Krista Varady

University of Illinois Chicago, Chicago, IL, United States

Objective: Concerns have been raised regarding the impact of time-restricted eating (TRE) on sex hormones in females. This study examined how TRE affects sex steroids in premenopausal and postmenopausal females.

Methods: This is a secondary analysis of an 8-week TRE study (4- to 6-hour eating window) conducted in adults with obesity. Men and perimenopausal females were excluded. Females were classified into two groups based on menstrual status: premenopausal (n = 12) or postmenopausal (n = 11).

Results: After 8 weeks, body weight decreased in premenopausal females (3% 2%) and postmenopausal females (4% 2%) (main effect of time, p <0.001), with no difference between groups (no group time interaction). Circulating levels of testosterone, androstenedione, and sex hormone binding globulin (SHBG) did not change in either group (no group time interaction). Dehydroepiandrosterone (DHEA) concentrations decreased (p <0.05) in premenopausal (14% 32%) and postmenopausal females (13% 34%; main effect of time, p = 0.03), with no difference between groups. Estradiol, estrone, and progesterone were measured only in postmenopausal females, and they remained unchanged.

Conclusions: In premenopausal females, androgens and SHBG remained unchanged during TRE, whereas DHEA decreased. In postmenopausal females, estrogens, progesterone, androgens, and SHBG did not change, but DHEA was reduced.

5:30 **Identification Of An Ionic Mechanism For E_{α} & Semi-Mediated Rapid Excitation In Neurons**

Yong Xu^{1,2,3}

¹USDA/ARS Children's Nutrition Research Center, Department of Pediatrics, Baylor College of Medicine, Houston, TX, United States, ²Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, TX, United States,

³Department of Medicine, Baylor College of Medicine, Houston, TX, United States

The major female ovarian hormone, 17 β -estradiol (E2), can alter neuronal excitability within milliseconds to regulate a variety of physiological processes. Estrogen receptor- α (ER α), classically known as a nuclear receptor, exists as a membrane-bound receptor to mediate this rapid action of E2, but the ionic mechanisms remain unclear. Here we show that a chloride channel protein, chloride intracellular channel protein-1 (Clc1), can physically interact with ER α with a preference to the membrane-bound ER α . Clc1-mediated currents can be enhanced by E2 and reduced by its depletion. In addition, Clc1 currents are required to mediate the E2-induced rapid excitations in multiple brain ER α populations. Further, genetic disruption of Clc1 in hypothalamic ER α neurons blunts the regulations of E2 on female body weight balance. In conclusion, we identified the Clc1 chloride channel as a key mediator for E2-induced rapid neuronal excitation, which may have a broad impact on multiple neurobiological processes regulated by E2.

Oral Session 3: Characteristics of Hyper- and Hypophagia

Chair(s): Kim Kinzig

4:15

Taste Reactivity In Mice: Disentangling Aversive And Anorexic Neural CircuitsMisgana Y. Ghidewon^{1,2}, Kuei-Pin Huang², Milena S. Almeida², Alisha A. Acosta², Amber L. Alhadeff^{1,2}¹University of Pennsylvania, Philadelphia, PA, United States, ²Monell Chemical Senses Center, Philadelphia, PA, United States

Glucagon like-peptide 1 receptor (GLP1R) agonists are currently the most effective treatments for obesity; however, nausea and vomiting remain common side effects that limit drug tolerance. Here, we developed an oro-facial taste reactivity assay in mice to determine how specific GLP1R neuron populations contribute to these side effects. We validated our ability to measure oro-facial responses to gustatory stimuli by showing that bitter taste, as well as flavors paired with aversive stimuli (lithium chloride or cinacalcet), produced aversive responses (gapes, chin rubs, and forelimb flails). We subsequently examined whether GLP1R neuron-induced aversion is independent of its feeding effects. Given that previous studies have shown that GLP1R populations within the dorsal vagal complex (DVC), including the area postrema (AP) and nucleus tractus solitarius (NTS), are key targets of GLP1R based drugs, we chemogenetically activated DVC GLP1R neurons, which induced aversive taste reactivity and food intake suppression. Interestingly, only chemogenetic activation of AP GLP1R neurons produced aversive responses, while NTS GLP1R neurons reduced feeding without inducing aversion. To determine whether these effects are mediated by distinct DVC GLP1R neuron projections, we optogenetically stimulated NTS GLP1R axons in the paraventricular hypothalamus (PVH), or AP GLP1R axons in the parabrachial nucleus (PBN). Stimulation of AP GLP1R to PBN projections induced aversive taste reactivity, while NTS GLP1R to PVH projections did not. Overall, these data reveal two discrete hindbrain GLP1R circuits: one mediating aversion and another mediating food intake suppression. These findings suggest NTS GLP1R to PVH neurons should be targeted by new obesity pharmacotherapies to minimize negative outcomes.

4:30

Compared To Glp-1R Mono-Agonism, Gipr/Glp-1R Dual Agonism Displays Sustained Anorexia And Body Weight Suppression With Reduced Incidence Of Gi Adverse Events In Preclinical Models.Tito Borner^{1,2,3}, Allison M Pataro¹, Sarah A Doebley¹, C. Daniel Furst¹, Xing Gao¹, Julia Halas¹, Allaha Mohiby¹, Minrong Ai⁴, Ricardo J Samms⁴, Bart C. De Jonghe^{1,2}, Matthew R. Hayes^{1,2}¹Department of Biobehavioral Health Sciences, University of Pennsylvania, Philadelphia, PA, United States, ²Department of Psychiatry, University of Pennsylvania, Philadelphia, PA, United States, ³Department of Biological Sciences, University of Southern California, Los Angeles, CA, United States, ⁴Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, United States

Glucose dependent insulinotropic polypeptide (GIP) and glucagon like-peptide 1 (GLP-1) are incretins that help orchestrate post-prandial glucose levels by augmenting insulin secretion. Current FDA-approved GLP-1 analogs are highly efficacious at normalizing glycemia and reducing body weight, however they elicit nausea and vomiting in a significant percentage of patients. Recent studies employing GLP-1/GIP dual analogs have yielded promising results in pre-clinical models and clinical trials, notably providing greater body weight loss and better glycemic control than GLP-1 receptor (GLP-1R) agonism alone. Intriguingly, GIP receptor (GIPR) activation reduces emetic responses following administration of the chemotherapeutic agent cisplatin in ferrets and shrews, suggesting potential broad anti-emetic effects. Here, we show in three different species (i.e., mice, rats and musk shrews) that a long-acting GIPR agonist blocks emesis and attenuates illness behaviors (e.g., conditioned taste avoidance and kaolin intake) elicited by GLP-1 receptor activation, while maintaining reduced food intake, body weight loss, and improved glucose tolerance. Importantly, the dual GLP-1R/GIPR agonist tirzepatide induced significantly less kaolin consumption in rats and emesis in shrews than equipotent doses of the GLP-1R mono-agonist semaglutide. This work supports the beneficial effect of combinatorial pharmaceutical strategies targeting both the GLP-1R and GIPR and suggest that such an approach may increase efficacy in treating obesity and diabetes also by reducing the severity and occurrence of nausea and vomiting.

4:45

Sex And Body Weight Determine Food Perceptions, Conflict, And The Probability Of Making Healthy Food Choices.Gabriela P. Larenas¹, Rene Baudrand¹, Victor Cortes¹, Bredford Kerr², Claudio E. Perez-Leighton¹¹Pontificia Universidad Catolica de Chile, Santiago, Chile, ²Universidad San Sebastian, Santiago, Chile

Why individuals struggle to make healthy food choices remains unclear. We aimed to analyze how individual characteristics influence food's attribute perception and choices. In an online study, 910 participants (BMI>30=17.3%; 32.3±11.4 years old; 57.3% female) completed surveys on demographics, dietary behavior, health, and lifestyle; rated food images for health and taste; and made food choices in healthy and typical contexts. Linear mixed models tested the effect of sex, BMI, and context on AUC (area under the curve derived from cursor trajectory), taste and health ratings, and percent of healthy choices. The influence of health and taste on healthy choices was analyzed by examining cursor trajectories and estimates from a dual drift-diffusion model based on reaction time (RT). Finally, a machine-learning (ML) approach was used to assess the importance of features in predicting AUC and the percent of healthy choices. We found that females, irrespective of their BMI, rated healthy foods as healthier and tastier than males. Still, participants with BMI≥30 made fewer healthy choices than those with BMI<30 in both contexts. Analyses of AUC, cursor trajectory, and RT showed that participants with BMI<30 made healthy choices based on health differences between food options, while participants with BMI≥30 made them based on taste differences. The ML approach showed that health and taste differences between options rather than participants' features predict AUC and healthy choices in a typical context. These data suggest that sex influences food perception while BMI influences the food choice process and outcome. Further, individual food environments appear more critical than individual characteristics in shaping food decisions and promoting healthier choices.

5:00

Sex Differences In Brain Activity And Functional Connectivity Impact Of Glp-1 And Amylin In Awake Rats.

Tanzil Arefin^{2,4,5}, Stina Borchers^{1,3}, Doris I. Olekanma^{1,2}, Morgan R. Sotzen^{1,2}, Suyeun Byun¹, Nanyin Zhang^{2,4,5}, Karolina P. Skibicka^{1,2,3}

¹Nutritional Sciences, Pennsylvania State University, State College, PA, United States, ²Huck Institutes of Life Science, Pennsylvania State University, State College, PA, United States, ³Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden, ⁴Department of Biomedical Engineering, Pennsylvania State University, State College, PA, United States, ⁵Center for Neurotechnology in Mental Health Research, Pennsylvania State University, State College, PA, United States

Gut-produced glucagon-like peptide-1 (GLP-1) and pancreas-made amylin produce potent reductions in ingestive behavior, by altering brain activity. While for both peptides a direct action in the hindbrain and the hypothalamus is expected, few rodent studies examine their impact on the whole brain activity, and those that do, test anesthetized male rats. However, both sex and anesthesia may significantly alter the influence of feeding controlling molecules on brain activity. Therefore, here we set out to investigate the effect of GLP-1 and amylin on brain activity and functional connectivity (FC) in awake adult male and female rats using resting-state functional magnetic resonance imaging (rsfMRI). Rats were habituated in a mock scanner over one week, and then tested with in-scanner intraperitoneal infusions of vehicle, GLP-1, and amylin. Subsequently, each rat was returned to their home-cage and food intake was measured for 1h to examine the relationship between the effects of the feeding peptides on ingestive behavior and brain activity, as well as FC. Very little overlap in brain activation patterns by GLP-1 or amylin was found between males and females. FC matrices also indicated a sex divergent effect of amylin and GLP-1. Most importantly correlation analysis between FC and feeding behavior revealed that different brain areas potentially drive reduced food intake in male and female rats. Our findings underscore the distributed and distinctly sex divergent neural network engaged by each of these anorexic peptides and suggest that different brain areas may be the primary drivers of the feeding outcome in male and female rats. Our data further highlight prominent activity and FC alterations in brain areas not typically associated with feeding behavior in both sexes.

5:15

Neural Responses To Anticipating And Receiving Monetary Rewards Is Associated With The Development Of Binge Eating In Youth From The Adolescent Brain Cognitive Development Study

Lindsay Bodell¹, Cassandra Lowe²

¹Western University, London, ON, Canada, ²University of Exeter, Exeter, United Kingdom

Binge eating is defined as eating a large amount of food and feeling out of control while eating. This behavior is a key diagnostic feature of several eating disorders and is associated with significant distress and impairment. Research using neuroimaging methods has suggested that increased responsivity within reward regions of the brain (e.g., ventral striatum (VS), ventral medial prefrontal cortex (vmPFC), orbitofrontal cortex (OFC), caudate) to the anticipation or receipt of rewards is associated with binge eating. However, limited longitudinal data has precluded understanding of the role of reward responsivity in the development of binge eating. We used data from the Adolescent Brain Cognitive Development® (ABCD) study to assess whether heightened neural responsivity to the anticipation and receipt of monetary rewards predicted the presence of binge eating two years later. Analyses focused on a subgroup of participants (N=1006; 45% female) with high negative urgency scores at age 9 or 10 years and who denied binge eating, in order to examine vulnerability processes. Heightened VS and OFC response to the anticipation of monetary rewards predicted the presence of binge eating at age 11 or 12 years (β s =.007-.008; p s<.01; d s=.23-.28). Moreover, heightened responses in the VS and caudate to receiving monetary rewards were associated with binge eating two years later (β s =.007-.012; p s<.001; d s=.25-.42). Analyses were pre-registered, and findings support a potential role of reward-related processes in the development of binge eating behaviors during adolescence.

5:30

The Neural Correlates Of Anxiety To Eat In Anorexia Nervosa

Kimberly R. Smith¹, Sarah H. Guo¹, Luiyi Chen¹, Joseph McGuire¹, Jeffrey Brunstrom², Timothy H. Moran¹, Arnold Bakker¹, Angela Guarda¹

¹Department of Psychiatry and Behavioral Sciences, Johns Hopkins School of Medicine, Baltimore, MD, United States,

²School of Psychological Science, University of Bristol, Bristol, United Kingdom

Anxiety to consume calorically dense foods is increasingly recognized as a contributing factor to the maintenance and relapse of Anorexia Nervosa (AN). Despite extensive research on general anxiety in AN, empirical evidence on eating-related anxiety remains limited. Therefore, we aimed to characterize eating-related anxiety and identify its neural correlates in AN. Acutely ill women with AN (N=18) and women of healthy weight and without a lifetime history of an eating disorder (HC; N=29) viewed images of higher (HED) and lower (LED) energy dense foods and rated their anxiety to consume each food on a visual analogue scale (VAS; anchors: 0=no anxiety, 100=most anxiety ever experienced) while being scanned in a 3 Tesla magnetic resonance imaging scanner. Behaviorally, reported anxiety to eat HED and LED foods was higher in AN relative to HC, with both groups reporting greater anxiety to eat HED compared with LED foods. Preliminary neuroimaging analyses aligned with the behavioral results. Greater activation in the amygdala and less activation in the caudate was observed in response to HED foods, and greater activation in the posterior cingulate cortex (PCC) and less activation in the insula was observed in response to LED foods in AN relative to HC. Greater activation in limbic regions (amygdala, PCC) and reduced activation in the caudate and insula indicate altered emotional processing of and motivation toward food stimuli, and potential difficulties in regulating emotional responses to anxiety-inducing food stimuli in AN. Interventions targeting fear inhibition and emotional regulation specific to food-related anxiety may be beneficial in optimizing outcomes for individuals with AN.

6:30 - 8:00 PM	Offsite
New Investigator Event	

The new investigator social is an opportunity for graduate students and post-docs to network. Food and bowling will be available to the first 60 participants. Drinks will be available for purchase. Please RSVP here: <https://forms.gle/ricqYw94SY4iMWwY8>. The event is at Pinstripes (435 East Illinois Street).

Thursday, July 11, 2024

8:00 - 7:15 PM

Sheraton Promenade West

Registration

8:30 - 10:15 AM

Riverwalk A

Poster Session 2 & Exhibits

P200

Examining Effects Of An Online Infant Sleep Intervention On Parenting And Infant Feeding And Eating

Stephanie Anzman-Frasca^{1, 2}, Juliana Goldsmith¹, Amanda Hassinger¹, Jennifer Savage³, Vaishali Gupta¹

¹Department of Pediatrics, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY, United States, ²Center for Ingestive Behavior Research, University at Buffalo, Buffalo, NY, United States, ³Department of Nutritional Sciences, the Pennsylvania State University, University Park, PA, United States

Establishing healthy infant sleep promotes well-being and may support healthy eating. We designed an interactive online sleep intervention that has been shown to increase infant sleep duration. In this analysis, we examine its effects on aspects of parenting and infant feeding and eating. Seventy-four first-time parents of infants (54% male, 50% white, 32% Black) were randomized to a sleep intervention or matched control focused on general baby care. Both interventions were delivered weekly from infant age 2 to 4 months as videos, infographics, and social support in private online groups. Parents completed online surveys at baseline (infant age ~6 months, midpoint (3 months), post-intervention (4 months), and follow-up (7 months). Parent stress, self-efficacy, satisfaction, and routines were measured longitudinally. Feeding practices and nutritional quality of infant intake were assessed at follow-up. ANOVAs were used to examine effects of study group and time and tested intervention engagement (whether parents joined their online group) as a covariate. 81% of parents engaged in the intervention. Parenting satisfaction increased in both groups ($p < .05$), with no group difference. There was a trend where the sleep group had higher use of routines, which became significant when adjusting for engagement ($p < .05$). There were no effects on parent stress, self-efficacy, or infant feeding or eating, although those who engaged in the intervention (across study groups) used coercive feeding practices less often (pressure, restriction; $p < .001$) and reported higher nutritional quality of intake ($p < .001$). Results highlight potential intervention impacts on aspects of parenting and child eating. Parallel support provided in the control arm may have dampened sleep intervention effects.

P201

Salivary Protein Upregulation Is Dependent On Functional Bitter Taste Signaling And Stimulus Intensity

Verenice Ascencio Gutierrez¹, Emily Demieri¹, Kimberly F. James¹, Laura E. Martin², Kyle Zumpano³, Kristin E. Kay⁴, Kathryn F. Medler⁵, Ann-Marie Torregrossa^{1,6}

¹Department of Psychology, University at Buffalo, Buffalo, NY, United States, ²The Coca-Cola Company, Atlanta, GA, United States, ³School of Biological Sciences, The University of Oklahoma, Norman, OK, United States, ⁴Lerner College of Medicine, Cleveland Clinic, Cleveland, OH, United States, ⁵School of Animal Sciences, Virginia Tech, Blacksburg, VA, United States, ⁶Center for Ingestive Behavior Research, University at Buffalo, Buffalo, NY, United States

We have demonstrated that exposure to a tannin acid- and quinine-containing diet upregulates salivary proteins (SP) in rats which reduce the salience of the bitter stimulus. Because sensory stimulation precedes SP changes, it is assumed that taste receptor activation is responsible for the outcome. However, no studies have 1) assessed whether functional taste signaling is necessary or 2) determined what aspects of diet exposure contribute to SP induction. We used B6 WT, and "taste blind" TRPM5 and TRPM4/5 KO mice to determine whether functional bitter taste signaling is important for SP upregulation. Mice were fed a diet containing either tannic acid (TA; 5%) or a control diet. All genotypes showed decreases in intake when given tannin diet compared to controls (p 's $< .05$). We interpret these data as the KO mice are still responsive to the astringency in TA as we expect no change in somatosensation with either KO. WT mice showed increased SP expression in several bands (p 's $< .05$) while KOs showed no changes in SP expression. These data suggest normal taste responding is necessary for SP upregulation. In our second experiment, to determine whether SP upregulation is dependent on stimulus intensity, we examined SP expression in rats following exposure to various concentrations of a quinine diet (0.125%, 0.25%, or 0.375%) or a non-bitter control. We saw a quinine concentration-dependent effect at the 14 kDa band ($p < .05$) and an overall effect of quinine diet at the 19, 23, 25, and 35 kDa bands (p 's $\leq .05$). These data suggest that some SP upregulation is concentration dependent.

P202

Does Menu Calorie Labelling Contribute To Eating Disorders? A Rapid Evidence Synthesis

Jane Brealey, Rebecca Evans, Amy Finlay, Thomas Gough, Megan Polden, I Gusti Ngurah Edi Putra, Loukia Tzavella, Rozemarijn Witkam, Eric Robinson
University of Liverpool, Liverpool, United Kingdom

Mandatory calorie labelling on menus was introduced in the Out of Home Food Sector in England in April 2022. However, menu calorie labelling has received public criticism since its implementation, due to the potential negative impacts on people with diagnosed eating disorders. We conducted a rapid evidence synthesis on studies that have collected data on this topic. This perspective synthesises qualitative and/or quantitative evidence on the potential impact of calorie labelling on people living with eating disorders. Through electronic database searches we identified a total of five eligible studies. In

recent quantitative studies measuring policy support (N=3 studies), between 43% and 85% of participants with eating disorders supported policy introduction. A smaller number of quantitative studies found that a significant proportion of participants with eating disorders reported potential worsening of eating disorder symptoms due to calorie labelling. In one study 55% reported that calorie labelling may worsen their eating disorder symptoms, and in another 91% stated that they had experienced challenges because of calories on menus. From qualitative studies (N=4), recurrent themes were identified. People with eating disorders felt that calorie labelling may lead to a hyper-fixation on calories, restrict food freedom and lead to feelings of anxiety, guilt and shame around eating. A small number of perceived benefits to calorie labelling were also identified by people with eating disorders. A limited number of studies suggest that although people with eating disorders tend to support calorie labelling as a public health policy, many feel that it also has potential to worsen their current symptoms or promote relapse. Measures to minimise potential harm are required.

P203

Exploring The Role Of Liking Of Taste In Satiation Across Multiple Laboratory Studies

Paige M. Cunningham, Kathleen L. Keller, Barbara J. Rolls

The Pennsylvania State University, University Park, PA, United States

We examined how changes in liking of the taste of a food as it is eaten relate to satiation. In this secondary analysis we combined data from 10 laboratory studies that assessed intake and ratings of liking of taste (on a 100 mm VAS) of a food before and after it was eaten. The dataset includes 2655 meals and 529 adults (30% men, age 18-68 y, 70% healthy weight). Analyses used linear mixed models with repeated measures accounting for study and food characteristics. Across studies, the mean pre-meal rating of taste was 71 ± 17 mm, and the mean post-meal rating was 52 ± 22 mm. Thus, while both pre- and post-meal ratings varied by study ($p < 0.02$), on average across studies, liking of taste declined during consumption, and individuals stopped eating when liking approached neutral (~ 50 mm). This suggests that eating continues until food is only neutrally liked. We propose that if a food continues to be liked throughout a meal, individuals will consume more. This is supported by our findings that across meals, pre-meal and post-meal ratings of liking of taste were independently positively associated with intake ($p < 0.02$); thus, individuals consumed more when initial liking was high, and when liking remained high. Additionally, change in liking of taste per gram was negatively related to intake ($p < 0.0001$); across meals, less was eaten when the change in liking per gram was smaller. Overall, these findings highlight the role of liking of taste in satiation, demonstrating that across meals individuals typically stopped eating at a neutral point in liking. Moreover, our findings suggest that risk of overconsumption may be higher at meals where liking of the taste of food is maintained throughout, for example when foods are initially highly liked or promote a smaller change in liking per gram.

P204

The PortionSize&Trade; Smartphone App: Testing Validity In Free-Living Conditions For Estimating Children'S Consumption Of Myplate Food Groups

Hanim E. Diktas¹, Sanjoy Saha^{1,2}, Chloe P. Lozano^{1,3}, Stephanie T. Broyles¹, Amanda E. Staino¹, Corby K. Martin¹, John W. Apolzan¹

¹Pennington Biomedical Research Center, Baton Rouge, LA, United States, ²Texas A&M Agriculture, Food, and Nutrition Evidence Center, Fort Worth, TX, United States, ³University of Hawaii at Manoa, Honolulu, HI, United States

The PortionSize (PS) smartphone app provides users with real-time feedback on MyPlate food group intake, which may help modify children's dietary intake to meet recommendations. This free-living study tested: 1) the validity of food group estimates from PS compared to the validated Digital Photography of Foods Method (DP) and 2) user satisfaction with the PS app. During two consecutive days, parents (n=28) recorded their children's (aged 7-12 y) food intake using PS for at least one meal and one snack per day. Parents measured portion size of foods and drinks by using embedded portion templates in the PS app. The app then automatically estimated dietary intake using templates and a built-in nutrient database. The app also transmitted the food images to trained raters who quantified intake using DP (criterion measure). PS app usability and satisfaction were assessed using a survey. Equivalence was evaluated with two one-sided t-tests ($\pm 25\%$ bounds). Most children were boys (57%), 25% had overweight or obesity. Parental estimates of children's food group intake using the PS app were not statistically equivalent to estimated intake by raters using DP (all $p > 0.14$). While error rate ($\pm SD$) was small for fruits, dairy and vegetables (error rate: 0.02 ± 0.7 , 0.06 ± 0.4 , -0.17 ± 0.7 servings; respectively), it was more meaningful for grain and protein (0.7 ± 1.7 and 0.5 ± 1.9 servings). Most participants rated PS with the two most favorable ratings for satisfaction (86%) and ease of use (82%). In free-living conditions, PS did not produce equal food group estimates compared to DP. However, many errors were small, and user satisfaction with PS indicates its potential for monitoring and improving children's dietary intake in real-time.

P205

Effects Of An Optimal Default Grocery Shopping Intervention On The Nutritional Quality Of Dietary Intake Patterns

Karlie Gambino¹, Mackenzie J. Ferrante^{1,2}, MacKenzie Swanson¹, Lily McGovern¹, Leonard Epstein¹, Stephanie Anzman-Frasca¹

¹University at Buffalo, Buffalo, NY, United States, ²Rutgers University, New Brunswick, NJ, United States

The prevalence of type 2 diabetes is increasing and while dietary changes are crucial, adherence to a healthful diet is difficult. In a 5-week pilot trial, a "Defaults" grocery shopping intervention improved the nutritional quality of grocery purchases among adults with or at risk for type 2 diabetes. This analysis sought to examine if the Default intervention affected participants' dietary intake. 55 participants were randomly assigned to 1 of 3 groups: Grocery shopping in person (Control), online (Online), or with an online, pre-filled cart (Defaults). All groups received diabetes-friendly recipes consistent with the Dietary Approaches to Stop Hypertension (DASH) diet (3/wk; weeks 2-4). The Defaults group's online grocery carts were pre-filled with recipe ingredients, which participants could modify. Participants grocery shopped in-person in week 1, as assigned in week 2-4, and as preferred in week 5, submitting grocery receipts weekly. Participants completed 1 food frequency questionnaire (FFQ) after week 5, assessing their typical intake for the prior 30 days (weeks 2-5). Nutritional quality scores were created from participants' FFQs by scoring adherence to 8 DASH indicators (e.g., carbohydrates). ANOVAs tested the effect of study group on the nutritional quality of intake patterns. No significant effect of study group on nutritional quality of dietary intake emerged, though results were in the expected direction when controlling for participants' income and gender (Control, $x = 20.9$; Online, $x = 21.1$; Defaults, $x = 22.0$; $p = 0.07$). Future research utilizing

objective measures of dietary intake, such as digital food photography, over time can augment our understanding of the effects of optimal defaults grocery shopping interventions on dietary intake.

P206

Parent Stress, Ethnicity, And Income Are Associated With Parent Readiness For Change For Treatment Of Childhood Obesity

Lauren N. Hamel, Ellen K. Pasquale, David R. Strong, Kyung E. Rhee, Dawn M. Eichen, Miekko P. Pretlow, Kerri N. Boutelle
University of California San Diego, San Diego, CA, United States

Parents are the agents of change and critical to treatment of children with overweight and obesity (OW/OB). However, parent readiness to change varies, and their ability to support their child in making healthy changes could be affected by their own mental health and demographic factors. 289 parents (m age=41.4 yr; 86.5% OW/OB; 90.3% female; 48.1% Latino, 35.6% non-Latino White, 16.3% Other) seeking treatment for their child with OW/OB (m age=10.0 yrs; m BMIZ=2.1) completed baseline questionnaires for 2 treatment studies evaluating readiness for change (Parent Readiness for Change Questionnaire; PRFCQ), depression (Center for Epidemiologic Studies Depression Scale- Revised; CESD-R), anxiety (Patient-Reported Outcomes Measurement Information System Anxiety Scale-8; PAS), stress (Parent Stress Scale; PSS), and demographics. Linear regression analyses examined associations between parent mental health and PRFCQ Importance, Confidence, and Readiness, controlling for parent age, gender, race, ethnicity, body mass index (BMI), child age, child BMIZ, and family income. PSS was positively associated with PRFCQ Importance ($\beta=0.03, p=0.04$). Latino parent ethnicity was negatively associated with PRFCQ Importance ($\beta=-1.01, p=0.01$). Family income was positively associated with PRFCQ Readiness ($\beta=0.02, p=0.03$). Analyses examining CESD-R and PAS with PRFCQ scales showed no relationships ($p>0.30$). In this sample of parents of children with OW/OB, parenting stress and ethnicity were related to importance for making healthy changes and family income was related to readiness for making healthy changes. As these factors affect program implementation, our findings support the need to develop interventions to target the unique needs of those with diverse backgrounds.

P207

Intergenerational Binge Eating-Like Behavior And Stress In The Juvenile Period

Elin Kachuki Dory¹, Avi Gueta², Yoni Loterstein¹, Lital Moshe¹, Devorah Matas³, Lee Koren³, Aron Weller^{1,2}

¹Department of Psychology, Bar Ilan University, Ramat Gan, Israel, ²Gonda Multidisciplinary Brain Research Center, Bar Ilan University, Ramat Gan, Israel, ³Faculty of Life Sciences, Bar Ilan University, Ramat Gan, Israel

Binge eating (BE) is consuming large amounts of food in a short time, while experiencing loss of control overeating behaviour. BE has a hereditary component, and juvenile stress (JS) may contribute to its onset and/or severity. We examined the impact of JS on BE-like behavior in adulthood, in an animal model of intergenerational BE. Twenty-four randomly assigned female Wistar rats received 2-hour access to palatable food (PF; Oreo Cookies) 3 or 5 times a week (3TW or 5TW) for 4 weeks. Afterwards, rats underwent the open field test (OFT), and hair samples were collected. At postnatal day (PND) 27-29, the offspring (124 females) either underwent JS (O-JSC) or not (control, CC). At PND 51-53, all offspring were tested in the OFT, dark/light box (DLB), and elevated plus maze (EPM) to assess stress/coping levels. At PND 70-85, offspring received 2-hour access to PF three times a week to assess their tendency to engage in BE-like behavior. Offspring's hair samples were collected afterwards. Compared to 5TW, 3TW had a greater binge size and more anxiety-like behaviours in the open field test (OFT), but hair corticosterone (CORT) levels did not differ. In the EPM and DLB, only in O-JSC, offspring of 3TW (O-3TW) spent less time in the open arms and lit area compared to O-5TW. O-3TW consumed more PF than O-5TW, and O-JSC consumed more than O-CC. In O-CC, O-3TW had lower hair CORT levels compared to O-5TW. This novel animal model highlights the complex interplay between parental and offspring's experience underlying psychopathology.

P208

Hedonic Value Of Salt In Children From The Province Of Cordoba And Its Relationship With The Perinatal Environment

Micah Leshem¹, Carolina Aurora², Barbara Belaver², Cintia Porcari³, Cristina Lencina³, Andrea Godina^{2,3}

¹University of Haifa, Haifa, Israel, ²Faculty of Psychology, National University of

Córdoba, Córdoba, Argentina, ³Ferreyra Institute, INIMEC-CONICET-UNC, Córdoba, Argentina

We evaluated in children from the province of Córdoba whether there are changes in the hedonic value of salt related to perinatal hydroelectrolytic alterations. An increase in the hedonic value (preference) of salt has been reported in association with maternal vomiting during pregnancy. After signing (parents or guardians) or providing oral informed consent, 150 children aged 9-11 years from two schools in the province of Córdoba, completed questionnaires to determine demographics, perinatal and dietary characteristics. The study was broad including other variables; here we present the significant associations of recalled pregnancy nausea and vomiting with offspring children's preference and intensity of oral sprays of 3 concentrations of salt scored by VAS. We show in the offspring respectively for none, medium, or high maternal pregnancy nausea, decreased taste intensity of 2.56M NaCl: 8.73 ± 0.41 (se), 8.91 ± 0.41 , 7.37 ± 0.46 ($p=0.01$, 1-way ANOVA); and increased preference for 0.09M NaCl: 4.20 ± 0.42 , 5.26 ± 0.44 , 6.50 ± 0.70 ($p<0.02$). Maternal vomiting during pregnancy also increased preference for 0.09M NaCl: 4.29 ± 0.38 , 6.08 ± 0.55 , 5.56 ± 0.64 ($p<0.02$). A similar pattern of effects emerged in the first trimester (not shown). The results confirm in Argentinian children of mothers suffering nausea or vomiting during pregnancy, reduced intensity and increased preference for salt solutions, similar to reports in the USA and Israel. We suggest that such early effects could contribute to salt consumption, a concern because throughout the world salt is consumed in excess according to WHO recommendations, increasing chronic non-communicable disease.

P209

Sex Differences In The Impact Of Food Cue Reactivity On Eating In The Absence Of Hunger In Children

Sara Maksi, Travis Masterson, Kyle Hallisky, Kathleen Keller
The Pennsylvania State University, University Park, PA, United States

Responsivity to external food cues has been posited as a risk factor for excess consumption and obesity, but supporting data has primarily come from questionnaires. Previous research has also found sex differences in the extent to which eating

behaviors are driven by external cues, with girls showing stronger relationships than boys. We tested the hypothesis that children's food cue reactivity- measured by the external food cue reactivity questionnaire (EFCR)- would be positively associated with eating in the absence of hunger (EAH), but this relationship would be stronger for girls than boys. Parents of children enrolled in a longitudinal study completed the nine-item EFCR. After an *ad libitum* meal and exposure to either food or toy commercials, EAH was measured by providing children with a variety of energy dense, palatable foods for a 10-minute free access period. The sample included 65 children (87.6% White) without obesity (BMI%<90), with an average age of 8.2 (± 0.8) years. Linear regression controlling for child BMI z-scores showed that EFCR was not significantly associated with the difference in EAH intake following food vs. toy conditions. However, the association between EFCR and EAH intake differed by sex ($p = 0.02$), such that for girls a 1 unit increase in EFCR was associated with a 27 kcal increase in EAH ($p = 0.25$) while for boys, a 1 unit increase in EFCR was associated with a 64 kcal decrease in EAH ($p = 0.07$). This finding supports previous research showing that child sex influences the relationship between food approach behaviors and obesity. Further research is needed to explore the relationships between sex differences in food cue reactivity and risk for obesity in children to develop more effective, tailored interventions.

P210

Examining Observed Mealtime Parenting In A Restaurant Setting

Emily McCray¹, Sara Tauriello¹, Jess Haines², Leonard H. Epstein^{1,3}, Lucia A. Leone^{3,4}, Stephanie Anzman-Frasca^{1,3}

¹Department of Pediatrics, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY, United States, ²Department of Family Relations and Applied Nutrition, University of Guelph, Guelph, ON, Canada, ³Center for Ingestive Behavior Research, University at Buffalo, Buffalo, NY, United States, ⁴Department of Community Health and Health Behavior, School of Public Health and Health Professions, University at Buffalo, Buffalo, NY, United States

Mealtime parenting may differ from general parenting strategies. Studies on this topic rarely examine parenting in a restaurant setting. We conducted a live-coded, observational pilot study to examine mealtime parenting at a regional quick service restaurant chain. Our objective was to describe observed mealtime parenting behaviors and compare these to self-reported general parenting. Twenty-six parent-child dyads (76.92% mothers; 96.15% non-Hispanic white; child age 4-8 years) were observed from a nearby table for 5 minutes before and 5 minutes during one evening meal using the Dyadic Parent-Child Interaction Coding System (DPICS), which measured counts of positive (e.g., reflection, praise), neutral (e.g., questions), and negative (e.g., commands) parent verbalizations. General parenting was measured via online survey using the Parenting Dimensions Inventory-Short Version. Average frequency/minute was calculated for each DPICS scale across pre and during meal observations. Correlations tested relationships between observed and self-reported parenting. The most frequent parenting behaviors observed were neutral talk ($M = 2.79 \pm 1.89$), questions ($M = 0.92 \pm 0.85$), and commands ($M = 0.31 \pm 0.32$). Self-reported and observed parenting were not significantly correlated, except for a positive association between observed commands and reported nurturance ($r = 0.45, p = .02$). All parents reported a positive (84.6%) or neutral (15.4%) experience participating in the observation, supporting the feasibility of conducting mealtime observations in a restaurant setting. Results suggest parenting in restaurants may be distinct from general parenting, warranting additional research on this topic in larger, more diverse samples and a consideration of implications for parenting interventions.

P211

The Role Of Salivary Proteins In Differentiating Toxic Vs. Non-Toxic Bitters

Kamila D. Nixon¹, Verence Ascencio Gutierrez¹, Samantha L. Brooker¹, Ann-Marie Torregrossa^{1,2}

¹Department of Psychology, University at Buffalo, Buffalo, NY, United States, ²Center for Ingestive Behavior Research, University at Buffalo, Buffalo, NY, United States

Plants contain bitter compounds, known as plant secondary compounds (PSCs), as a defense mechanism against herbivory. These chemicals are sometimes safe to consume (heathy vegetables) but can also be bioactive or toxic. We have shown animals increase intake of tannic acid (TA) and quinine-containing diets after repeated exposure, in part due to changes in salivary proteins (SPs) decreasing the bitterness of the stimulus. We have also demonstrated that acceptance of a known safe stimuli (quinine) does not generalize to acceptance of a potentially toxic bioactive compound (caffeine) despite the chemical similarities between them. Here we ask if exposure and acceptance to a "toxic" compound increases acceptance of a chemically similar safe compound. We used brief-access tests to measure taste-driven responses to tannic acid (TA), epigallocatechin gallate (EGCG), and denatonium (DB) before and after SPs were manipulated by exposure to TA. Rats were tested on a control diet, then half were switched to a 3% tannic acid diet, and all animals were retested. We found that rats exposed to a 3% TA diet showed a trend in acceptance for EGCG (EC_{50} : $p=0.06$). These data combined with our previous data suggest SPs may be facilitating rats' ability to differentiate and increase acceptance of a safe bitter after exposure to a "toxic" bitter, but not vice versa.

P212

Executive Functions As A Predictor Of Eating Behaviors In Young Adults

Maria Rego¹, Emma Leslie^{2,3}, Benjamin Katz⁴, Emily Schmall¹, Kevin P. Davy¹, Valisa Hedrick¹, Alexandra DiFeliceantonio^{1,2}, Brenda Davy¹

¹Department of Human Nutrition, Foods, and Exercise, Blacksburg, VA, United States, ²Fralin Biomedical Research Institute, Virginia Tech, Roanoke, VA, United States, ³Graduate Program in Translational Biology, Medicine, and Health, Virginia Tech, Blacksburg, VA, United States, ⁴Department of Human Development and Family Science, Virginia Tech, Blacksburg, VA, United States

Executive functions (EF), including inhibitory control, working memory, and cognitive flexibility, play a crucial role in the decision-making and self-regulation processes involved in eating behaviors. This study aims to determine which EF domains best predict eating behavior measured via a self-reported questionnaire and an *ad libitum* buffet meal. This is part of an ongoing cross-over controlled-feeding trial comparing ultra-processed foods (UPF) with non-UPF. This preliminary analysis includes 15 adults (53% female), aged 18-25 years. Before beginning the 2-week controlled eucaloric diet, participants completed 1) the Three-Factor Eating Questionnaire (TFEQ) to assess restrained, uncontrolled, and emotional eating behaviors, and 2) computerized EF tasks (i.e., Corsi-block tapping backwards for working memory, the Flanker task for selective attention and interference control, and the Go/No-Go task for inhibitory control). After the 2-week controlled diet, an *ad libitum* buffet meal was used to evaluate food consumption and meal energy intake. A 4-week washout took place

between diets. Linear regression analyses were used to assess associations between cognitive performance and TFEQ domains and *ad libitum* buffet meal intake. There were inverse associations between the Corsi score and the No-Go accuracy with meal eating rate ($p < 0.05$, $R^2 = 0.23$ and $R^2 = 0.19$, respectively), but not food consumed. These associations were observed independent of diet condition. In addition, inverse associations were noted between the Corsi score and No-Go accuracy with dietary cognitive restraint on the TFEQ ($p < 0.01$, $R^2 = 0.29$ and $R^2 = 0.26$, respectively) and for the No-Go accuracy and emotional eating on the TFEQ ($p < 0.01$, $R^2 = 0.15$). These findings suggest that working memory and inhibitory control might be important EF domains linked with eating behaviors when *ad libitum* food is available.

P213

Amylin Receptor Signaling In The Laterodorsal Tegmental Nucleus Controls Food Intake Through A Neurotensin Projection To The Ventral Tegmental Area.

Marcos Sanchez-Navarro¹, Samantha Fortin¹, Carlie Zhang¹, Halcyon Hu¹, Gina Leininger², Matthew Hayes¹

¹University of Pennsylvania, Philadelphia, PA, United States, ²Michigan State University, East Lansing, MI, United States

Despite the distributed nature of CNS amylin receptors, research on the role of amylin signaling in the control of energy balance has been focused on brainstem and hypothalamic nuclei, leaving other calcitonin receptor (CTR) expressing nuclei such as the mesopontine laterodorsal tegmental nucleus (LDTg) understudied. Our lab has shown that activation of LDTg CTR (LDTg^{CTR}) neurons reduces feeding and that endogenous LDTg CTR signaling is important for energy balance, as evidenced by increased food intake and body weight gain following LDTg CTR knockdown. However, the downstream targets of LDTg^{CTR} cells mediating these feeding effects remain unknown. In this study, we anatomically characterize LDTg^{CTR} neurons and demonstrate that a subpopulation projects to the ventral tegmental area (VTA) and leads to increased activation of VTA neurons. Additionally, we use a dual virus approach to show that a unilateral circuit specific (LDTg --> VTA) CTR-KD is sufficient to attenuate the anorexigenic effects of peripherally-delivered salmon calcitonin (sCT), a calcitonin receptor agonist. Moreover, LDTg neurons are known to produce neurotensin (Nts), a neuropeptide known to act in the VTA to reduce food intake. However, whether LDTg^{CTR} --> VTA neurons produce Nts has not been explored. Here we use a pharmacological approach to explore the relationship between CNS CTR signaling and Nts receptor signaling in the VTA. Our results show that Nts receptor antagonism in the VTA is sufficient to attenuate the anorexigenic effects of ICV administered sCT. Altogether, our results functionally characterize a novel signaling pathway in the control of energy balance and establishes a relationship between LDTg CTR signaling and VTA Nts receptor expressing cells. Support: NIDDK105155

P214

Effect Of Hydration Status On Palatable Food Intake

Wan Hei So¹, Kenny, Chi Kin Ip², Zhi Yi Ong¹

¹School of Psychology, University of New South Wales, UNSW Sydney, Australia, ²Children's Cancer Institute, University of New South Wales, UNSW Sydney, Australia

Water and food intake are interdependent such that food intake is typically accompanied by prandial drinking while dehydration reduces food intake. However, whether this ingestive behaviour persists or becomes dysregulated when energy dense, palatable food is available, is unclear. This study therefore aims to examine the interaction between water and palatable food intake. Rats were given acute (n=12) or chronic (n=8) exposure to high-fat diet (HFD) and, water and food intake were measured during euhydration, dehydration and rehydration. Brains of rats maintained on chow or HFD after euhydration, dehydration and rehydration were collected to determine the impact of HFD on neural activity under different hydration status. Results showed that when dehydrated, rats with acute HFD exposure did not suppress food intake. However, in rats with chronic exposure to HFD, dehydration reduced HFD intake. Interestingly, HFD intake remained low during rehydration. This was in contrast to chow-maintained rats which showed an increase in food intake during rehydration. Water intake in chronic HFD rats were also significantly lower than chow-maintained rats. Quantitation of c-Fos expressing cells revealed that dehydration increased c-fos expressing cells in the supraoptic nucleus (SON) in both chow and HFD-maintained rats, albeit less c-Fos cells in the HFD-maintained rats. In the nucleus of the solitary tract (NTS), rehydration increased c-fos expressing cells only in chow-maintained rats, but not HFD-maintained rats. In summary, hydration status differentially affects food and water intake in HFD and chow-maintained animals. These effects could be mediated in part by differences in neural activation in SON and NTS. Current work is exploring other contributing nuclear substrates.

P215

The Impact Of Ultra-Processed Food Consumption On Eating Behaviors Over 12 Months In Children

Dabin Yeum¹, Sarah Ann Duck², Gita Thapaliya², Susan Melhorn¹, Ellen Schur¹, Susan Carnell², Leticia Sewaybricker¹

¹University of Washington, Seattle, WA, United States, ²Johns Hopkins University, Baltimore, MD, United States

Background: Ultra-processed foods (UPF) are often energy-dense and nutrient-poor, and excess consumption could contribute to the development of childhood obesity. This study examined the relationship between baseline UPF intake and 12-month changes in eating behaviors in children. **Methods:** Parents completed 3 unannounced dietary recalls via ASA-24 at baseline and the Child Eating Behavior Questionnaire (CEBQ) at baseline and 12-month follow-up visits (N=65). The daily average % of calories from UPF and unprocessed/minimally processed foods (MPF) were calculated using the NOVA Food Classification system. The ratio of % calories from UPF to MPF was calculated to create the relative overall daily consumption of UPF. Linear regression evaluated the association between baseline UPF intake ratio and 12-month changes in 7 subscales of appetitive traits, adjusting for sex and BMI z-score. **Results:** At baseline, mean age and BMI z-score were 10.6 (SD 0.92) and 1.0 (SD 1.03); 43% were female. Mean ratio of baseline UPF to MPF consumption was 3.2 (SD 2.3). There were no cross-sectional associations between child's UPF intake ratio and eating behaviors at baseline. Greater baseline UPF intake ratio was independently associated with 12-month changes in CEBQ desire to drink ($\beta = 0.026$, $p < .05$) and food responsiveness subscales ($\beta = 0.021$, $p < .05$) after adjusting for covariates. Baseline UPF intake ratio was not associated with changes in other CEBQ subscales. **Conclusion:** UPF consumption predicted increases in obesogenic eating behaviors of desire to drink and food responsiveness, independent of child's body adiposity. Further research could investigate whether different types of UPF, e.g., sugar-sweetened beverages, exacerbate subsequent obesogenic appetitive traits in children.

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Daily Erythritol Intake Over Five Weeks Did Not Affect Glycemic Control In Healthy AdolescentsAnita Altstaedt^{1,2}, Valentine Bordier^{1,2}, Emilie Flad^{1,2}, Juergen Drewe³, Christoph Beglinger^{1,2}, Anne Christin Meyer-Gerspach^{1,2}, Bettina Woelnerhanssen^{1,2}¹St. Clara Research Ltd. at St. Claraspital, Basel, Switzerland, ²Faculty of Medicine, University of Basel, Basel, Switzerland, ³Department of Clinical Pharmacology and Toxicology, University Hospital Basel, Basel, Switzerland

INTRODUCTION Worldwide 18% of all children and adolescents have overweight or obesity. A reduction of sugar intake is recommended as prevention of obesity. This can be achieved through partial substitution of sugar with alternative sweeteners such as the non-caloric bulk-sweetener erythritol. **METHODS** We included 30 healthy, lean adolescents (15/group) in this randomized, double-blind parallel trial. They received either 18 g erythritol or 12.5 g sucrose dissolved in 150 mL tap water twice daily for 5 weeks. Blood samples were collected at fixed time points during an oral glucose tolerance test to analyze glycemic control (glucose, insulin, HOMA-IR) before and after the intervention period. During the week before and the final week of intervention, food intake was assessed by food records. **RESULTS** In the erythritol-group we found i) parameters of glycemic control were not significantly different; ii) total sugar ($p = 0.034$) and total carbohydrate intake ($p = 0.038$) were significantly reduced; iii) total caloric intake ($p = 0.068$) showed a trend of reduction after the intervention period. In the sucrose group we found i) Cmax blood glucose was not significantly different; ii) Cmax insulin ($p = 0.030$) and HOMA-IR ($p < 0.001$) were significantly increased; iii) total sugar intake ($p = 0.073$) showed a trend of increase; iv) no significant differences in total carbohydrate and total caloric intake after the intervention period. **CONCLUSION** Daily erythritol intake over a 5-week period led to a significant reduction in total sugar and carbohydrate intake, not affecting glycemic control. Contrarily, sucrose intervention led to a significant increase in maximum blood insulin concentrations and HOMA-IR. Erythritol appears as feasible sugar alternative in healthy adolescents.

P217

Exogenous Satiety Liver/Gut Hormone Leap2 Dose Dependently Reduces Blood Ketones Without Changes In Serum Insulin Or Gh In Adults Without ObesityRaghav Bhargava¹, Marcela Rodriguez-Flores¹, Sandra Luur¹, MIMOZA Emini¹, Wanqian Li¹, Wai I Ng¹, Xinyi Zhang¹, Jialin Guo¹, Jiaxun Liu¹, James Minnion², Anthony P Goldstone¹¹PsychoNeuroEndocrinology Research Group, Division of Psychiatry, Department of Brain Sciences, Imperial College London, London, United Kingdom, ²Department of Metabolism, Digestion and Reproduction, Imperial College London, London, United Kingdom

Background: Liver/gut satiety hormone LEAP2, inverse agonist at the growth hormone secretagogue receptor (GHSR), is reciprocally regulated to acyl ghrelin (AG). Fasting increases blood AG, ketones/free fatty acids (FFA) and GH, and lowers serum insulin, mimicked by supraphysiological exogenous AG administration (PMID 23533240). Exogenous LEAP2 infusion (25 pmol/kg/min) increased fasting insulin, and reduced GH, glycerol and FFA in men without obesity (PMID 35492241). This suggests GHSR signalling increasing lipolysis, but this may be direct or indirectly via changes in insulin and GH. **Methods:** Single-blind, placebo-controlled, within-participant study in adults without obesity who received 5.7h intravenous infusion of saline or LEAP2 (12, 24, 36 pmol/kg/min) after an overnight fast, with 71kcal snack at 195min. Plasma AG, glucose, serum insulin, GH, cortisol, lipids and venous β -hydroxybutyrate (BHB) assayed at 4-7 time points, and pituitary hormones at baseline and 310min. Linear mixed model analysis for correlation of LEAP2 dose with changes in blood measures. **Results:** Adults without obesity (age 26-55 years, BMI 19.1-23.9 kg/m²) attended for total of 12 infusions ($n=3$, 2 men). LEAP2 dose negatively correlated with venous BHB (incremental AUC -10- 310min: $r^2=0.36$, β -1.38 mmol/L.min, $P=0.033$; post-prandial iAUC 195-310min $r^2=0.20$, $P=0.033$). There were no significant correlations with iAUC glucose, insulin, GH, cortisol, triglycerides for either time period, nor changes in free thyroxine, TSH, prolactin ($P>0.05$). **Conclusion:** Intravenous LEAP2 infusion dose dependently reduced fasting venous BHB, independent of changes in serum insulin and GH. These preliminary findings support a direct effect of GHSR signalling to stimulate lipolysis in adults without obesity.

P218

Transcranial Random Noise Stimulation Over The Dlpfc Reduces Food Craving.

Seolha Lee, Hyung Jin Choi

Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul, South Korea

Objectives: The DLPFC is crucial in food intake regulation. Using tES to target the DLPFC offers potential weight loss benefits. While past studies highlighted appetite reduction with tDCS on the DLPFC, research on tRNS in this context is limited. Our aim is to investigate tRNS efficacy on the DLPFC in reducing appetite in young, healthy adult females. **Methods:** This study utilized a parallel, double-blind, randomized, sham-controlled design. Sixty women aged 20-39 years with a BMI of 18.5 or above participated, excluding those on weight or appetite-affecting medication. Participants were randomly assigned to receive either sham treatment or tRNS in a 1:1 ratio over the 2-week intervention period. Each visit included 20 minutes of tES session (tRNS; 2mA, 100~500Hz). Appetite Visual Analog Scale (VAS) assessments were conducted before and after each tES session. Furthermore, assessments included anthropometric measurements, administration of questionnaires (STAI-S, STAI-T, DEBQ, BDI-2, BIS-11-R, EES, YFAS 2.0, PSS), and cognitive behavioral tasks (go/nogo task, food rating task). **Results:** After tRNS treatment, emotional eating significantly decreased, showing a statistically significant difference compared to the sham group. Additionally, hunger, prospective food consumption, and desire to eat significantly decreased in the tRNS group post-treatment, while fullness and satiety significantly increased. **Conclusions:** This study provides evidence that repetitive tRNS applied to the DLPFC effectively reduces emotional eating and decreases food craving. These results lend support to further investigations into the application of tRNS in the management of obesity.

P219

Circulating Agouti-Related Peptide, Unrestricted Eating And Cognitive Dietary RestraintLisa L. Morselli, Samuel Lawton, Roland James, Srividya Kidambi
Medical College of Wisconsin, Milwaukee, WI, United States

Agouti-related peptide (AgRP) neurons are key components of the melanocortin system and regulate hunger. They also project to the medial prefrontal cortex, an area involved in cognitive dietary restraint, and to the hedonic system, where they modulate dopamine release. AgRP is also found in plasma and was suggested as a potential marker of central melanocortinergic tone. Circulating AgRP (cAgRP) is lower in subjects with obesity and increases with weight loss, indicating it may promote hunger after weight loss. We hypothesized that higher cAgRP promotes lower cognitive dietary restraint (CDR) and higher unrestrained eating (UE) measures after weight loss. Ten adults with obesity (age 37 ± 11 y, BMI 35.4 ± 4.9 kg/m²) were enrolled in a lifestyle-based weight loss intervention. cAgRP was assayed in plasma at baseline and 2 months. CDR, UE and emotional eating (EmE) were measured with the Three-Factor Eating Questionnaire (v18) at both timepoints. Results (means $\pm$ SD) were compared by unpaired t-test with significance set at $p < 0.05$. At 2 months, significant weight loss (defined as 5% loss from baseline) was achieved by 5 subjects (weight loss group [WLG] $8.2 \pm 1.6\%$ vs weight maintenance group [WMG] $1.4 \pm 2.3\%$, $p < 0.001$). cAgRP increased by $9 \pm 20\%$ in WLG and decreased by $11 \pm 7\%$ in WMG ($p = 0.07$). CDR, UE and EmE scores did not differ by group at baseline. CDR score increased by $28 \pm 11\%$ in WLG vs $5 \pm 18\%$ in WMG ($p = 0.04$). UE and EmE scores declined similarly in both groups. A trend for positive correlation between changes in CDR score and cAgRP was seen overall ($r = 0.584$, $p = 0.08$). Contrary to our hypothesis, preliminary results suggest a greater CDR in those with greater cAgRP increases during weight loss. No correlation between cAgRP and UE scores was found.

P220

A Novel Microbial Sensing Gut-Brain Pathway Regulates Feeding Behavior

Alfahdah Alsudayri, Madelyn McDevitt, Jiangjiang Zhu, Devin Peterson, Lihua Ye
The Ohio State University, Columbus, OH, United States

Feeding behavior is well-conserved among all organisms and is regulated by hormonal and neuronal signals. Gut microbiota regulates feeding behavior. However, the molecular mechanisms underlying it remain unclear. Endogenous opioid peptides, such as Enkephalin (Enk), are associated with food pleasure and the hedonic eating process. Using the single-cell RNA sequencing approach in the zebrafish model, we discovered that a subset of Enteroendocrine cells (EECs) in the intestine epithelium highly and specifically express Enk. These Enk+EECs express Transient receptor potential ankyrin 1 (Trpa1), a membrane receptor that senses chemical stimulants from many food spices. Loss of EEC Enk signaling reduces food interest and food intake. Using an optochemical approach to stimulating the ENK+ EECs and in vivo vagal calcium imaging, our data demonstrate that photoactivation of these Enk+EECs in the small intestine stimulates a subset of vagal sensory neurons. Interestingly, the ENK+EEC-activated vagal sensory neurons do not sense nutrients. Our previous study demonstrates that microbial tryptophan metabolites such as indole or indole-3-aldehyde (I3A) are novel agonists for Trpa1 receptors. Activating the Trpa1-expressing Enk+EECs through microbial tryptophan metabolites increases the dopaminergic and serotonergic neuronal activities in the caudal hypothalamus, a brain region that promotes eating motivation and food intake in zebrafish. Treating zebrafish with microbial tryptophan metabolite indole before the meal increases food intake. Together, our data suggests that the gut bacteria may secrete microbial tryptophan metabolites to stimulate the Trpa1-expressing Enk+EECs to modulate vagal and hypothalamus neuronal activity to promote feeding motivation and food intake.

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Glucagon Gene (Gcg) Knockdown Rats Display Increased Preference For Palatable Food And Drinks In A Sex-Dependent Manner

Michelle B. Bales, Inge E. Guerrero, Eva H. Rucinski, Linda Rinaman
Florida State University, Tallahassee, FL, United States

Overconsumption of palatable foods high in fat and sugar contribute to the obesity crisis, and it is important to understand how brain circuits control food choice and regulate total caloric intake. Given evidence that glucagon-like peptide-1 (GLP1) receptor signaling reduces palatable food intake, we predicted that homozygous Gcg-Cre rats [a novel Gcg (including GLP1) knockdown (KD) model; 10.1016/j.molmet.2022.101631] should display increased preference for and intake of palatable substances. To test this, Gcg-KD rats (N=6/sex) and wild type controls (WT; N=5-6/sex) were given 8 wks ad libitum home cage access to a choice between Western diet (WD; 41% fat, 29% sugar; Research Diets) and regular chow. Compared to WT controls, Gcg-KD female rats (but not males) displayed increased preference for WD vs. chow ($p = 0.04$). In a second experiment, the chow-maintained rats (N=8 Gcg-KD/sex; N=4-6 WT/sex) were given two-bottle preference tests over two consecutive days for each of six sucrose concentrations (0.03-1M). Compared to WT controls, male Gcg-KD rats (but not females) consumed more sucrose and displayed greater preference for sucrose vs. chow as a caloric source ($p < 0.0001$). Similar results were obtained during subsequent access to chocolate Ensure over two days: Gcg-KD male rats (but not females) drank significantly more Ensure than WT controls (N=6F, 4M). Overall, these results support the view that endogenous Gcg-encoded peptides, including GLP1, serve to limit rats' preference for (and intake of) palatable foods and drinks, with apparent sex differences depending on the type of palatable substance available.

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Differential Modulation Of Mesolimbic Dopamine Signaling To Sucrose Versus Fat By Vta Amylin Receptor Activation

Rohan V. Bhimani^{1,2}, Lily Rzepecki², Jinwoo Park^{1,2,3}, Elizabeth G. Miettlicki-Baase^{1,4,5}

¹Neuroscience Program, University at Buffalo, Buffalo, NY, United States, ²Biotechnical and Clinical Laboratory Sciences, University at Buffalo, Buffalo, NY, United States, ³Pharmacology and Toxicology, University at Buffalo, Buffalo, NY, United States, ⁴Exercise and Nutrition Sciences, University at Buffalo, Buffalo, NY, United States, ⁵Center for Ingestive Behavior Research, University at Buffalo, Buffalo, NY, United States

Amylin is a peptide hormone that suppresses feeding and weight gain via actions in the central nervous system. The ventral tegmental area (VTA), a dopaminergic nucleus in the mesolimbic reward system, is a key central site of action for the hypophagic effects of amylin receptor (AmyR) activation. Previous work has shown that microinjection of the AmyR agonist salmon calcitonin (sCT) into the VTA reduces intake of fat and sugar solutions, with more potent suppression of fat intake under some experimental conditions, and also suppresses phasic dopamine signaling in the nucleus accumbens core (NAcC) in response to random sucrose pellet delivery. However, it is unknown whether this dampening of NAcC dopamine by VTA AmyR activation also occurs in response to other palatable foods. Here, we used fast-scan cyclic voltammetry in male rats to test the hypothesis that VTA injection of an AmyR agonist would reduce NAcC dopamine signaling in response to intraoral (IO) delivery of isocaloric fat or sucrose solution. At baseline, IO fat elicited a greater NAcC dopamine response than did an IO delivery of isocaloric sucrose. When VTA AmyR were activated via sCT, the dopamine responses to each

solution were attenuated, but the reduction in dopamine was greater for fat than sucrose. These findings strengthen our understanding of the neural underpinnings of the hypophagic effects of VTA AmyR signaling and also highlight a potential neurochemical mechanism by which VTA AmyR activation differentially reduces intake of palatable fluids.

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Regulation Of The Melanocortin-4 Receptor (Mc4R) By Attractin Like Protein 1 (Atrnl1).

Paul Buscaglia^{1,2,3,4}, Julien Sebag^{1,2,3,4}

¹Department of Molecular Physiology and Biophysics, Carver College of Medicine, Iowa City, IA, United States,

²F.O.E.D.R.C, Iowa City, IA, United States, ³Pappajohn Biomedical Institute, Iowa City, IA, United States, ⁴Iowa Neuroscience Institute, Iowa City, IA, United States

The Melanocortin-4 Receptor (MC4R) plays a central role in the regulation of energy homeostasis. Mutations in MC4R are responsible for up to 6% of early onset obesity in humans and deletion of MC4R in mice results in severe obesity due to hyperphagia. MC4R is a GPCR expressed in different region of the brains including the paraventricular nucleus of the hypothalamus. Stimulation of MC4R by its agonist aMSH and inhibition by its endogenous inverse agonist AGRP result in inhibition or stimulation of food intake respectively. MC4R is known to interact with two single transmembrane proteins, the Melanocortin Receptor Accessory Protein 2 (MRAP2) and Attractin Like Protein 1 (ATRNL1). Whereas MRAP2 has been shown to promote MC4R signaling in vitro and in vivo, the pharmacological and physiological relevance of ATRNL1 for MC4R signaling and actions is not known. In this study, we show that ATRNL1 interacts with MC4R, potentiates its signaling and inhibits b-arrestin recruitment to the receptor. To assess the physiological importance of ATRNL1, we generated ATRNL1^{Flox} mouse model. Deletion of ATRNL1 in MC4R neurons resulted in hyperphagia and increased body weight both on standard and high fat diets. Deletion of ATRNL1 in MC4R neurons also resulted in a decreased activation of those neurons in response to injection of the MC4R agonist MTII. Our results identify ATRNL1 as an important regulatory protein of MC4R and a required component of the energy homeostasis machinery.

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The Influence Of Alcohol And High Fat Diet In Female Humanized Apoe4 Knockin Rats

Chan Young Choi¹, Sarah/M Rauch¹, Jassmyr/J Venegas¹, Mythili Machireddi¹, Nu-Chu Liang^{1,2,3,4}

¹Department of Psychology, University of Illinois Urbana Champaign, Champaign, IL, United States, ²Neuroscience

Program, University of Illinois Urbana Champaign, Champaign, IL, United States, ³Division of Nutritional Sciences,

University of Illinois Urbana Champaign, Champaign, IL, United States, ⁴Carl R. Woese Institute for Genomic Biology, University of Illinois Urbana-Champaign, Champaign, IL, United States

The most prevalent genetic risk factor for the late onset Alzheimer's disease (AD) is the E4 allele of Apolipoprotein E (ApoE4). Previous studies have utilized transgenic mouse models to investigate neurobiological mechanisms underlying the increased risk of ApoE4 in AD. Compared to mice, however, rats may better recapitulate neuropathology in AD because of their similar tau isoforms to humans. Given that the ApoE4 risk for AD is worse in females than males, we evaluated the interaction between ApoE4 and modifiable AD risk factors, alcohol and high fat diet exposure, in wildtype (WT) and humanized ApoE4 knockin (E4) Sprague-Dawley female rats (n = 13 – 16/genotype, 13-month-old). We first examined conditioned aversion learning and extinction with 10% sucrose and alcohol (1.5 g/kg, i.p.) as the conditioned and unconditioned stimulus, respectively. Subsequently, oral glucose (2 g/kg) and insulin (1 U/kg) tolerance was assessed respectively after 4 and 10 days of 40% high fat diet feeding. Upon initial exposure, E4 rats consumed significantly less sucrose than their WT counterparts. Contrasting previous finding in mice, aversion learning and extinction in WT and E4 rats did not differ. WT rats reached higher peak levels of plasma glucose than did the E4 rats, but the levels returned to baseline 2 hours after the gavage in both genotypes. Similarly, no genotype-dependent difference in insulin tolerance was observed. These results suggest that female rats expressing human ApoE4 do not become more susceptible to alcohol and high fat diet challenge compared to WT rats. Future studies should determine whether these findings persist when comparing rats with a knockin allele that carries a reduced, neutral, or increased risk for AD i.e., the E2, E3 and E4 alleles.

P225

Trap2-Dreadd Mice For Analyzing Conditioned Taste Aversion: Role Of Lithium-Activated Cells

Jason M. Cote, Thomas A. Hought

Florida State University, Tallahassee, FL, United States

While a useful correlate of neuronal activity, c-Fos expression alone does not establish the functional contribution, if any, of cells to behavioral effects of visceral stimuli such as LiCl during acquisition of conditioned taste aversion (CTA). We bred and validated TRAP2 (Targeted Recombination in Active Population) mice expressing DREADDs (Designer Receptors Exclusively Activated by Designer Drugs) in c-Fos-positive cells, which allows permanent genetic access to the cells activated by acute LiCl. TRAP2 mice (*Fos*^{2A-iCreER}) expressing tamoxifen-inducible Cre recombinase without disrupting endogenous c-Fos (Denardo et al. 2019) were bred with mice with either inhibitory (R26-hM4Di/mCitrine) or excitatory (R26-hM3Dq/mCitrine) floxed DREADDs, generating *Fos*^{2A-iCreER}-hM4Di or *Fos*^{2A-iCreER}-hM3Dq mice (n=12-24). DREADD expression was induced by intraperitoneal injections of LiCl or NaCl (40ml/kg, 0.15M, ip) paired with 4-hydroxytamoxifen (4-OHT; 50mg/kg) or sesame oil (5ml/kg) at 1 hour. Two-three weeks later *Fos*^{2A-iCreER}-hM4Di mice were given 10-min access to saccharin paired with LiCl (40ml/kg, 0.15M, ip) and CNO (3 mg/kg, ip). Additional *Fos*^{2A-iCreER}-hM3Dq mice were given 10-min saccharin paired with CNO alone (3 mg/kg). All mice were given 10 days of 2-

bottle tests of saccharin vs water. In mice expressing the inhibitory DREADDs, CNO injection blocked CTA acquisition, with higher saccharin preference than control LiCl-injected mice. In mice expressing the excitatory DREADDs, CNO alone failed to induce CTA. We conclude that full LiCl activation of c-Fos-expressing cells is **necessary** for CTA acquisition, but that re-activation of those cells alone when paired with saccharin is not **sufficient** for CTA acquisition.

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Adolescent Morphine Administration And Withdrawal Persistently Decreases Reward Sensitivity And Heightens The Effects Of Adulthood Re-Exposure

Rachel M Donka, Deaglan A McAndrew, Sema M Patel, Maxine K Loh, Mitchell F Roitman, Jamie D Roitman
University of Illinois Chicago, Chicago, IL, United States

Adolescent substance abuse drives lasting changes in reward processing and decision making. To determine the effects of adolescent opioid treatment and withdrawal on reward sensitivity, we used a rate-frequency (RF) intracranial self-stimulation (ICSS) paradigm in adolescent (n=26) rats. Rats were implanted with stimulating electrodes (PN28) in the medial forebrain bundle at the level of the lateral hypothalamus and trained twice daily to perform a variant RF ICSS task tailored for adolescents. Morphine (5 mg/kg) or saline (0.5 ml/kg) was injected prior to the AM ICSS session from PN 45-51. Sessions continued to PN60 to measure withdrawal, after which rats were trained on a standard adult RF ICSS task. Both groups underwent morphine administration (10mg/kg) from PN90-96 and were monitored through withdrawal. In adolescent controls, reward sensitivity was stable across baseline, injection, and post-injection sessions. Adolescent morphine administration resulted in a significant increase in reward sensitivity relative to baseline in AM sessions, but a decrease in PM sessions that remained suppressed for the entire 9-day withdrawal period. Adulthood re-exposure resulted in a greater increase in sensitivity during administration but a more profound suppression in withdrawal relative to controls. Controls mirrored a separate group of adults (n=14) that showed significantly increased reward sensitivity during morphine administration, followed by a decrease during withdrawal that returned to pre-administration levels within 3 days. In sum, adolescent morphine exposure has long-term effects on reward sensitivity that may drive susceptibility to maladaptive behaviors in adulthood. Further research will examine potential mechanisms of these shifts and effects on decision making.

P227

Autonomic Physiological Responses Of The Glucagon-Like Peptide-1 Receptor Agonist Exendin-4 Are Mediated Through Direct Action In The Locus Coeruleus

Samantha M Fortin, Halcyon Hu, Maggie Zhou, Matthew R Hayes
Department of Psychiatry, University of Pennsylvania, Philadelphia, PA, United States

The locus coeruleus (LC), the major noradrenergic nucleus of the brain, regulates diverse aspects of physiology and behavior. Despite its known contribution to autonomic function, behavioral arousal, and recently food intake control, the LC remains an underexplored area of the brain in the context of energy balance. Our work has demonstrated that LC glucagon-like peptide-1 receptors (GLP-1Rs), expressed on presynaptic glutamate terminals, can be pharmacologically stimulated with the GLP-1R agonist exendin-4 (Ex-4; 0.05 mg) to suppress food intake and body weight in the rat. Given the well-established role of the LC in regulating sympathetic and parasympathetic output, here, we explored the LC as a site of action for various changes in autonomic physiology associated with Ex-4. Microinjections of Ex-4 to the LC suppressed gastric emptying and induced tachycardia, hypothermia, and produced acute hyperglycemia similarly to published responses observed following ICV Ex-4. Pretreatment with the GLP-1R antagonist exendin- (9-39) (Ex-9; 10 mg) delivered to the LC prior to intraperitoneal Ex-4 (5 mg/kg) completely abolished Ex-4-induced hyperglycemia, suggesting that the LC is a site of action for sympathetically mediated increases in blood glucose. Modest increases in corticosterone levels associated with LC Ex-4 suggests that the physiological effects observed in our studies are not consequent of a stress response. Ongoing investigations are focused on characterizing LC projections engaged by LC Ex-4 to impact sympathetic and parasympathetic outflow with tracing, immunohistochemical and chemogenetic strategies. This work will contribute to a better understanding of the role of the LC in autonomic control and the mechanisms underlying LC Ex-4-induced food intake suppression.

P228

The Gliotransmitter Octadecaneuropeptide As A Therapeutic Target For Energy Balance Control

Caroline E. Geisler¹, Halcyon Hu¹, Drew Belser¹, Kylie Chichura², Tito Borner^{1,3}, Robert P. Doyle², Matthew R. Hayes¹

¹University of Pennsylvania, Philadelphia, PA, United States, ²Syracuse University, Syracuse, NY, United States,

³University of Southern California, Los Angeles, CA, United States

The global obesity epidemic has accelerated in recent decades. Currently, the leading class of FDA-approved anti-obesity drugs targets the glucagon-like peptide-1 (GLP-1) receptor. However, patients on these medications encounter side effects including nausea/emesis and eventually hit a weight loss plateau. Therefore, more research is needed to improve the efficacy of current drug treatments. In this study, we explored the effects of octadecaneuropeptide (ODN), an anorexigenic gliopeptide, along with a synthetically designed analog TDN, to improve blood glucose and reduce body weight in rodents and shrews. We found that ICV injection of ODN decreased chow intake in lean rats, as well as high-fat-diet (HFD) intake and body weight in obese rats, with improved insulin sensitivity. In shrews, intraperitoneal (IP) injected ODN suppressed food intake without exhibiting emesis, suggesting that ODN does not induce gastrointestinal adverse events. When combined with an IP delivery of the GLP-1 analog liraglutide, ICV ODN enhanced food intake suppression and weight loss. To optimize the effects of ODN, we synthesized an ODN analog, TDN, that also decreased food intake and body weight when given ICV in rats. Furthermore, chronic delivery of IP TDN in obese mice suppressed HFD intake and reduced body weight without a weight loss plateau for 9 consecutive days. To validate a central site of action, using PET imaging, we visualized radiolabeled TDN after IP delivery in nude mice was largely accumulated in the brain, demonstrating blood brain

barrier permeability. These results suggest that ODN and its analog TDN may be an effective target for the treatment of obesity and diabetes as a stand-alone or combination therapy with GLP-1 therapeutics.

P229

Nicotine Exposure Augments Habitual Opioid Seeking: A Critical Role For The Dorsal Lateral Striatum

Sarah C Honeycutt, Ashmita Mukherjee, Cerissa E Shorter, Kajol V Sontate, Gregory C Loney
The State University of New York, University at Buffalo, Buffalo, NY, United States

Nicotine dependence is highly comorbid with opioid use disorders (OUDs). Approximately 85% of individuals in treatment for OUDs are habitual users of nicotine-containing products. Largely, OUDs are characterized by a habitual or compulsive drive to obtain and consume opioids despite clear adverse consequences. In both clinical and preclinical studies, this habitual opioid consuming phenotype is an emergent phenomenon that arises following prolonged and escalated opioid use. Drug seeking habits, or compulsivity, are often modeled in rodents with the heterogenous seeking-taking chain schedule of reinforcement. Here, rats are tasked with pressing a 'seeking' lever on a variable interval in order to gain access to a 'taking' lever which is responsible for intravenous delivery of drug. In the present study, we demonstrate that nicotine administration significantly increases both seeking ($F_{(4,40)} = 3.41, p < 0.05$) and taking ($F_{(4,40)} = 3.89, p < 0.01$) of the synthetic opioid fentanyl. Furthermore, this phenotype persists despite administration of foot shock punishment contingent on continued fentanyl seeking. As such, nicotine-exposed rats demonstrate a compulsive-like fentanyl consuming phenotype despite a limited drug history. In a separate group of rats, we performed excitotoxic lesions of the dorsal lateral striatum (DLS) prior to any drug experience. Preliminary data support that DLS lesions significantly suppress the ability for nicotine to promote escalated fentanyl consumption and early emergence of compulsive-like fentanyl seeking habits. Future studies are planned to elucidate downstream targets of the DLS in mediating this behavioral phenomenon. Specifically, we intend to evaluate the role played by the circuit connecting the insular cortex DLS.

P230

Loss Of Estradiol Promotes Greater Body Weight Dysregulation Than Exposure To High Fat Diet In Female Rats.

Savoya S. Joyner, Lisa A. Eckel
Florida State University, Tallahassee, FL, United States

Diet-induced obesity (DIO) is studied primarily in males despite clear sex differences in the neural control of feeding. The scant literature in females suggests they are less susceptible to DIO than males, with protection arising from estradiol (E2), which has been shown to attenuate the inflammation linked to weight gain in rodents fed high fat diet (HFD). To explore this hypothesis, we examined how loss of E2 affects food intake, weight gain, and hedonic eating. Food intake and body weight were monitored for 4 weeks in chow-fed ovariectomized (OVX) rats with or without E2 replacement (OVX-veh, OVX-E2). Control (ovarian intact) rats were fed chow or 45% HFD (INT-chow, INT-HFD). After 4 weeks, hedonic eating was assessed in a 30-min chocolate Ensure "dessert" test administered immediately after the consumption of a satiating meal. INT-HFD rats displayed a transient (7 day) increase in food intake relative to INT-chow rats, resulting in a small but reliable increase in body weight. Loss of E2 in OVX-veh rats increased food intake and weight gain relative to OVX-EB rats. Interestingly, chow-fed OVX-veh rats consumed more food and gained more weight than INT-HFD rats (4-week weight gain: 63.7 ± 2.4 g vs 35.2 ± 3.2 g). During the dessert test, OVX-oil rats also consumed more chocolate Ensure than INT-HFD rats (23.1 ± 1.3 vs 12.4 ± 1.3 kcal). We conclude that loss of E2 promotes greater body weight dysregulation and responsiveness to satiation signals, as assessed by a test of hedonic eating, than exposure to an obesogenic, HFD. Ongoing studies are assessing whether neuroinflammation contributes to the impairment in body weight regulation in chow-fed OVX rats.

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Role For Neurotensin Receptor 1-Expressing Neurons In The Lateral Preoptic Area In Ingestive And Pain Behaviors

Beenhwa Lee, Charlotte M Schultz, Raluca Bugescu, Geoffroy Laumet, Gina M Leininger
Department of Physiology, Michigan State University, East Lansing, MI, United States

Obesity reduces lifespan and increases risk of developing chronic pain. Injecting Neurotensin (Nts) or Neurotensin receptor 1 (NtsR1) agonists has pleiotropic effects, including restraining feeding, pain, and weight gain, suggesting that augmenting Nts-NtsR1 signaling might be useful to treat obesity and pain simultaneously. However, region-specific subsets of NtsR1-expressing neurons mediate distinct physiology, which has hindered understanding of where to leverage the Nts-NtsR1 system to specifically manage energy balance and/or pain. We identified NtsR1-expressing neurons in the lateral preoptic area (LPO^{NtsR1} neurons) that project to areas known to modulate feeding and pain, including the periaqueductal gray and ventral tegmental area. We therefore hypothesized that activating LPO^{NtsR1} neurons could reduce feeding and pain. To test this, we expressed excitatory Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) in LPO^{NtsR1} neurons of normal weight and obese mice. Mice were treated via cross-over design with vehicle (control) or the DREADD ligand CNO to activate the LPO^{NtsR1} neurons prior to assessment of ingestive, locomotor, and pain behaviors. In contrast to our hypothesis, activating LPO^{NtsR1} neurons had no impact on thermal, inflammatory, or obesity-induced pain. However, LPO^{NtsR1} neuronal activation blunted fasting-induced refeeding and thirst-induced drinking but this was not due to impaired locomotor activity in the normal weight mice. Excitingly, activating LPO^{NtsR1} neurons in obese mice also increased their locomotor activity and promoted weight loss. Taken together, these data implicate LPO^{NtsR1} neurons in selectively mediating the feeding and weight-reducing aspects of the Nts-NtsR1 system. Supported by the NIH and DOD.

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Mapping The Brain Feeding Circuitry Activated By Cagrilintide, Semaglutide And Cagrisema In Mice

Greta Lommi¹, Mohammed Hankir¹, Christelle Le Foll¹, Thomas A. Lutz¹, Anna Secher², Kirsten Raun²

¹Institute of Veterinary Physiology, University of Zurich, Zurich, Switzerland, ²Global Drug Discovery, Novo Nordisk A/S, Maaloev, Denmark

Cagrilintide, a long-acting amylin analogue, is in clinical development for obesity and type-2-diabetes. In combination with semaglutide (CagriSema), it demonstrates an additive effect on reducing body weight. However, the brain feeding circuitry targeted by these drugs remains poorly understood. We therefore assessed the acute effects of cagrilintide, semaglutide and CagriSema on food intake and neuronal activity in mice. In lean chow-fed C57BL/6 mice (n=6/group), intraperitoneal (I.P.) injections of cagrilintide (10 nmol/kg) reduced food intake compared to vehicle during the dark phase; semaglutide (10

nmol/kg) and CagriSema (2+2 nmol/kg) had a more potent effect compared to cagrilintide. cFos analysis of brains from chow-fed calcitonin receptor-Cre (CalcR)-tdTomato mice that received acute subcutaneous injections of vehicle (n=8/group), cagrilintide, semaglutide or CagriSema after a 12h fast, revealed activation of CalcR-expressing neurons in the hindbrain area postrema (AP) and nucleus tractus solitarius (NTS) for all compounds. Notably, only cagrilintide and semaglutide activated downstream projection sites in the lateral parabrachial nucleus (IPBN), a brain region known to promote aversion. Semaglutide and CagriSema also activated neurons in the arcuate nucleus of the hypothalamus (ARC). Our findings shed light on the brain feeding circuitry activated by cagrilintide, semaglutide and CagriSema, and suggest that CagriSema achieves potent appetite suppression at lower doses than treatments with single compounds without engaging aversive pathways. An ongoing study on chow-fed CalcR-tdTomato mice treated with the same compounds during the fed state, will provide further insights on the hypothalamic feeding circuitry activated by these agonists.

P233 **Early Life High-Fat Diet Drives Precocious Maturation Of Vagal Satiety Responses And Overconsumption Of Fats In Adulthood**

Meaghan E. McCoy^{1,2}, Anna K. Kamitakahara^{1,2,3}

¹Children's Hospital Los Angeles, The Saban Research Institute, Los Angeles, CA, United States, ²University of Southern California, Los Angeles, CA, United States, ³Keck School of Medicine, Los Angeles, CA, United States

Vagal sensory neurons (VSNs) transmit information about the satiating and rewarding properties of ingested foods from the intestines to the brain. However, the impact of early life nutrition on the development of VSN sensitivity remains poorly defined. To examine this, a mouse model was used to compare mice reared on either a chow (control) or high-fat (HFD^{EARLY}) diet through the lactation period, after which all mice were weaned onto chow. On postnatal day (P) 35 and in adulthood (P120), HFD^{EARLY} mice weighed more than control mice, demonstrating the lasting effects of early life HFD. To examine the contributions of VSN satiety signaling to this phenotype, mice were fasted overnight, injected with cholecystokinin (CCK), and presented with HFD. On P35, control mice exhibited highly variable responses to CCK, suggestive of immature satiety signaling at this age. By contrast, HFD^{EARLY} pups displayed a consistent decrease in food intake similar to adult responses, suggesting that early-life HFD drives precocious maturation of CCK satiety signaling. By P120, responses to CCK were equivalent between groups. To examine gut-brain vagal reward signaling, a two-bottle preference assay was used in which mice were given a choice between equicaloric solutions of lipid or sucrose. HFD^{EARLY} females consumed significantly more lipid and exhibited a higher preference for lipids than control females, demonstrating that early life exposure to HFD modifies post-ingestive reward processing. A similar trend was observed between control and HFD^{EARLY} males that did not reach statistical significance (p=0.06). These findings demonstrate that early-life exposure to HFD drives precocious maturation of CCK-dependent satiety signaling and has a lasting impact on the regulation of feeding behavior.

P234 **Hypothalamic Astrocyte Signalling: Influences On Food Intake Control And Systemic Energy Balance**

Keila Navarro i Batista, Christelle Le Foll

Institute of Veterinary Physiology, University of Zurich, Zurich, Switzerland

Neuronal nutrient sensing plays a critical role in the control of energy homeostasis. Specialised neurons in the mediobasal hypothalamus (MBH) respond to an ample range of nutrient-associated signals. Defects in this process are associated with metabolic imbalance, promoting obesity onset and development. In the MBH, astrocyte ketone body (KB) signalling has been suggested to modulated neuronal nutrient sensing, indirectly affecting whole-body metabolic as well. Early research from our group found that acute inhibition of ketogenesis in this hypothalamic area impairs food intake control against hypercaloric diet consumption. It is thus likely that astrocyte KB participates in the maintenance of energy homeostasis, allowing organism to adjust to hypercaloric feeding conditions. To further investigate this hypothesis, the following studies explored the metabolic role of MBH astrocyte fatty acid transporter 4 (FATP4) and of ketogenic enzyme HMG CoA lyase (HMGCL) in mice and rats, respectively. A GFAP-specific Cre-containing AAV was stereotactically delivered into MBH of FATP-flox mice. Under 45% HFD, knockout mice gain significantly more weight than controls. Interestingly, increased body weight did not stem from changes in food intake (which remained similar across groups) but from changes in energy metabolism. FATP4-depleted mice had lower energy expenditure values, accompanied by increased leptin levels, and decreased brown adipose tissue oxidation. The loss of HMGCL in MBH astrocytes of Sprague-Dawley rats promoted similar effects, increasing body weight, and decreasing energy expenditure and affecting thermogenesis. Overall, these observations provide a novel perspective on MBH astrocytes and their role in the control of energy homeostasis.

P235 **Intra-Nasal Delivery Of A Ghrelin Mimetic Engages The Brain Ghrelin Signalling System In Mice**

Renee Poelman, Iris Stoltenborg, Marie LeMay, Erik Schele, Suzanne Dickson

Department of Physiology/Endocrine, Institute of Neuroscience and Physiology, The Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden

Ghrelin is perhaps best known for its potent orexigenic effects engaging, for example, the agouti-related peptide (AgRP) neurones in the arcuate nucleus (Arc). It also activates growth hormone (GH)-releasing hormone neurones in this region, triggering pituitary GH release. Here, we investigated whether the brain ghrelin signalling system can be activated by

intranasal (IN) delivery of ghrelin receptor (GHSR) agonists in mice. In addition to ghrelin, we tested synthetic mimetics, namely GHRP-6 (a small peptide) and MK-0677 (a non-peptide). Of these, initial screening, enabled us to select GHRP-6 for focused investigation, based on its orexigenic effect. GHRP-6 (5 mg/kg, the pre-determined dose) increased food intake for 2 hours (H1 0.29±0.09; H2 0.11±0.03 gram) following IN administration relative to saline controls (H1 0.03±0.01; H2 0.04±0.02 gram) (n=9). This increase was reflected by increased meal frequency (saline: H1 1.3±0.5; H2 0.4±0.2 GHRP-6: H1 3.9±0.7; H2 1.4±0.3 meals) and size (saline: H1 0.02±0.01; H2 0.04±0.02 GHRP-6: H1 0.07±0.01; H2 0.07±0.01 gram). Blood serum GH levels were also increased (from 2.2±0.4 ng/ml in controls to 28±10 ng/ml after IN GHRP-6; n=10). Engagement of the brain ghrelin signalling system was also reflected by Fos activation of populations of Arc neurones (from 21±3 in controls to 36±6 cells/section with IN GHRP-6; n=12). RNAscope revealed that the activated populations included both AgRP (53%) and GHRH (9%) populations. Our data provide proof-of-concept that the brain ghrelin signalling system can be engaged by IN delivery of the ghrelin mimetic, GHRP-6.

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Glucose-Dependent Insulinotropic Polypeptide Receptor Agonism Modulates Interleukin-1B Induced Aversion And Parabrachial Neuron Activity

Haley Province^{1,2}, Nikolas Hayes¹, Carolyn Lorch¹, Hayley McMorrow¹, Jessica Xia¹, Lisa Beutler¹

¹Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, United States, ²Medical Scientist Training Program, Northwestern University Feinberg School of Medicine, Chicago, IL, United States

Glucose-dependent insulinotropic polypeptide (GIP) is a gut-derived incretin hormone that acts on GIP receptors (GIPR) distributed across the central nervous system to regulate energy homeostasis. Recent reports have demonstrated that central GIP signaling may also be anti-aversive. GIPR agonism attenuates nausea and vomiting induced by a glucagon-like peptide 1 agonist and prevents conditioned taste aversion due to a variety of unpleasant stimuli. However, the mechanism by which GIP signaling mediates anti-aversive effects during inflammation is not fully understood. The inflammatory cytokine interleukin-1β (IL-1β) is elevated in many inflammatory diseases and its ability to induce aversion is well-known. Here, we show that the GIPR agonist D-Ala²-GIP abrogates IL-1β-induced taste aversion. To study the neural substrates underlying this phenomenon, we looked at neuronal activity of a well-defined aversive node: calcitonin-gene related peptide-expressing neurons in the parabrachial nucleus (CGRP neurons). Our *in vivo* fiber photometry data demonstrate that IL-1β increases CGRP neural activity, and that this increase in neural activity is significantly attenuated by co-administration of D-Ala²-GIP. Taken together, these data suggest that the aversive effects of IL-1β are at least partially mediated by CGRP neurons and that GIPR agonism blunts the aversive effects of IL-1β via these neurons.

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A Vagal Influence On Schizophrenia? A Nationwide Retrospective Cohort Of Vagotomized Individuals.

Cornelia F Richter¹, Karolina P Skibicka^{2,3}, Urs Meyer¹, Sabine Rohrmann⁴, Jean-Philippe Krieger^{1,2}

¹Institute of Veterinary Pharmacology and Toxicology, University of Zurich-Vetsuisse, Zurich, Switzerland, ²Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden, ³Department of Nutritional Sciences, Pennsylvania State University, State College, Pennsylvania, PA, United States, ⁴Division of Chronic Disease Epidemiology, Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland

Rodent studies have implicated vagal signals as contributors to the development of schizophrenia-related abnormalities in brain and behavior. Whether the impairment of vagal communication is a risk factor for schizophrenia in humans remains, however, unclear. Vagotomy, the surgical lesion of the vagus nerve, was routinely performed as a treatment for peptic ulcer before modern therapeutic options were available. The primary objective of this study was to investigate whether vagotomy modulates the subsequent risk of developing schizophrenia. In a secondary goal, we considered diverse vagotomy techniques (i.e., truncal or selective), and tested whether the extent of denervation modulates the risk of schizophrenia. A nationwide retrospective matched cohort approach was applied. 8,315 vagotomized individuals were identified in the Swedish National Patient Register during the period 1970-2020 and 40,855 non-vagotomized individuals matched for age, sex and type of peptic ulcer. The risk of being diagnosed with schizophrenia and associated psychoses (ICD10 codes F20-29) was analyzed using Cox proportional hazards regression models, including death as competing risk. Overall, vagotomy was not significantly associated with schizophrenia (HR: 0.91 [0.72; 1.16]). However, truncal vagotomy significantly increased the risk of developing schizophrenia (HR: 1.69 [1.08; 2.64]), whereas selective vagotomy showed no significant association (HR: 0.80 [0.61; 1.04]). Our results support the hypothesis that vagal impairments modulate the risk of schizophrenia. As truncal but not selective vagotomy is associated with an increased risk of schizophrenia, the activity of subdiaphragmatic non-gastric vagal branches may be of particular relevance for the development of schizophrenia.

P238

Inflammation Mediates Binge Drinking Behavior In Drinking In The Dark Paradigm

Sean Schrank¹, Joshua P Sevigny^{1,2}, Nurfadhlin I Yunus¹, Katherine R Vetter¹, Mikaela Valchinova¹, Vivek Ily¹, Oscar D Aguilar¹, Dennis R Sparta^{1,2}

¹Department of Psychology, University of Illinois Chicago, Chicago, IL, United States, ²Graduate Program in Neuroscience, University of Illinois Chicago, Chicago, IL, United States

Alcohol use disorder (AUD) is devastating and commonplace within the United States, and persons suffering from AUD may struggle to maintain sobriety. The prevalence and prominence of a social culture of alcohol consumption masks the severity of AUD, and we are in need of improved therapeutic options. Many Americans report binge drinking monthly, and these binge drinking events often precede AUD but the mechanisms for conversion to AUD are not understood. The neuroinflammatory consequences of alcohol consumption are now being appreciated, and it has been previously demonstrated that immunomodulatory therapies such as minocycline decrease alcohol preference in 24-hour access models. Here we demonstrate that minocycline treatment reduces binge alcohol consumption in a repeat Drinking in the Dark (DID) model C57BL/6 mice without respect to sex. We observe no lasting effects of the minocycline treatment on food, water, or sucrose consumption alcohol, nor do we observe lasting effects on anxiety like behaviors measured 24 hours after alcohol binge. We analyzed microglial morphology and our preliminary observations suggest that immediately after binge drinking microglia display somatic hypertrophy, which is reversed by minocycline treatment. This lends credence to the idea that inflammation within the CeA caused by alcohol consumption potentiates binge drinking behaviors, and future work will address CRF+ neuron sensitivity to inflammation. This data suggests that immunomodulatory therapies are worth exploring

in the context of AUD, but more research is needed to understand the mechanisms by which inflammation and reward interact.

P239

Circadian-Dependent Changes In *Ghsr* (Ghrelin Receptor) Expression In The Mouse Suprachiasmatic Nucleus

Sepideh Sheybani Deloui¹, Omprakash Singh¹, Jeffrey Zigman^{1,2,3}

¹Center for Hypothalamic Research, Department of Internal Medicine, UT Southwestern Medical Center, Dallas, TX, United States, ²Division of Endocrinology and Metabolism, Department of Internal Medicine, UT Southwestern Medical Center, Dallas, TX, United States, ³Department of Psychiatry, UT Southwestern Medical Center, Dallas, TX, United States

The hormone ghrelin potently stimulates food intake. Its receptor, encoded by the *Ghsr* gene, is highly expressed in the suprachiasmatic nucleus (SCN), the light-entrainable regulator of cellular rhythms. Applying ghrelin to cultured SCN slices phase advances neuronal activity only at circadian time (CT) 6 (subjective day). Administering ghrelin analog phase delays SCN neuronal firing and circadian locomotor activity in mice only at CT12 (subjective night). How circadian changes in SCN *Ghsr* neurons influence these windows of ghrelin sensitivity is unclear. Here, we characterized spatiotemporal patterns of *Ghsr* expression by reanalyzing published scRNA-seq data from mouse SCNs at CT 7.5 (subjective day) vs. CT15.5 (subjective night), and data from SCNs obtained in the dark phase vs. after 1-hour of light. The majority (28.9%)

of *Ghsr*⁺ neurons were *Avp*^{high}; 22.5% were *Grp/Alcam*⁺. *Ghsr* expression was 25% higher at CT15.5 vs. CT7.5. *Ghsr* was the only upregulated gene at CT15.5 in the *Ghsr*⁺ AVP cluster, while 35 other genes including several “day-distinguishing” genes (*Prok*, *Rgs16*, *Dbp*) were downregulated. A 1-hour light impulse decreased *Ghsr* expression in AVP neurons by 23%.

GO-term analysis of CT-dependent expression changes in *Ghsr*⁺ cells showed enrichment in genes related to synaptic plasticity and GABAergic synapses (*Gabrg3*, *Syt17*, *Magi2*) during subjective night. RNAScope corroborated the co-expression of *Ghsr* with *Avp* and the CT-dependent change *Ghsr* expression in SCN. In sum, we found higher expression of *Ghsr* and genes involved in synaptic transmission especially in SCN AVP neurons during subjective night. This may underlie the previously reported disparate effects of ghrelin at different CTs. The impact of these changes on eating is yet to be studied.

P240

Genotype-Dependent Effects Of Uncontrolled Eating On Bmi And Brain Encoding Of Food

Justin J Sung^{1,2}, Xue S Davis², Chavonn R Duncan², Xi Fang², Jade Quillian², Sophie Mickus², Ioanna Panopoulou², Noah Koster², Marney A White², Carlos M Grilo², Dana M Small^{1,2}

¹McGill University, Montreal, QC, Canada, ²Yale University, New Haven, CT, United States

Individuals possessing a copy of the A1 allele of the taq1A polymorphism have decreased dopamine receptor subtype 2 (DRD2) density and show increased risk for obesity and addiction. A1 carriers (A1+) vs non carriers (A1-) also show opposing responses to food related stimuli in dopamine source and target areas. A recent study in mice reported that knock down of the gene associated with the polymorphism (ankyrin repeat and kinase domain containing 1 (Ank1) gene) decreases DRD2 expression and produces obesogenic phenotypes (including enhanced food motivation). Uncontrolled eating, measured using the Reward-based Eating Drive Scale 13-item Version (RED-13), is suggested to be a unifying heritable trait linked to obesity and overeating. In the present study, we tested the effect of genotype (A1+ vs A1-) on the relationship between uncontrolled eating and body mass index (BMI) and brain response to milkshake in 44 individuals (31 female). Genotype had a significant influence on the association between RED-13 scores and both BMI (p<0.001) and brain response to milkshake in the ventral striatum (p_{FWE}=0.032) and insula (p_{FWE}=0.029). Consistent with prior reports, associations were negative for A1+ individuals and positive for A1- individuals. These results demonstrate that the influence of uncontrolled eating on BMI and brain encoding of food depends on the taq1A polymorphism.

P241

Chemogenetic Activation Of D2/A2A-Expressing Medium Spiny Neurons In The Nucleus Accumbens Core Mirrors The Delaying Effect Of Novelty Exposure On Feeding Onset In Rats

Astrid A. S. van Irsen^{1,2,3,4}, Tess Kool^{1,2,3,4}, Rick Wenning^{1,2,3,4}, Margo Slomp^{1,2,3,4}, Ewout Foppen^{1,2,3,4}, Andries Kalsbeek^{1,2,3,4}, Anayanci MasÃfÃs-Vargas^{1,2,3,4}, Susanne E. la Fleur^{1,2,3,4}

¹Amsterdam UMC location University of Amsterdam, Endocrinology Laboratory, Dept Laboratory Medicine, Meibergdreef 9, Amsterdam, Netherlands, ²Amsterdam Neuroscience, Cellular and Molecular Mechanisms, Amsterdam, Netherlands, ³Amsterdam Gastroenterology Endocrinology & Metabolism, Amsterdam, Netherlands, ⁴Netherlands Institute for Neuroscience, an Institute of the Royal Netherlands Academy of Arts and Sciences, Amsterdam, Netherlands

The nucleus accumbens core (NAcc) is pivotal for locomotion, motivation, and reinforcement-driven learning. Almost all accumbal neurons are medium spiny neurons (MSNs) expressing either dopamine D1 receptors (D1) or a combination of dopamine D2 (D2) and adenosine Adora2a (A2a) receptors. Previous research showed that activating NAcc-D2 MSNs using Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) or a D2 agonist reduced locomotor activity without affecting 24h food intake. With a transgenic rat line expressing improved Cre (iCre)-recombinase in A2a-expressing neurons we replicated the decreased locomotor activity in rats (between t=90-240 min: p<0.05, n=9) using DREADDs to activate D2/A2a MSNs of the NAcc, however, also a 30 min delay in feeding onset was observed (between t=45-75m: p<0.002, n=9). Next, our objective was: 1) to inhibit these cells to observe the opposite effect and 2) investigate if the delay in feeding onset could be explained by a novelty-induced latency. We selectively inhibited A2a/D2 MSNs in the NAcc by using iCre dependent DREADDs and an i.p. injection of Clozapine N-Oxide (CNO; 2 mg/kg). Rats were 8h-fasted during the end of the light-phase, received CNO or saline (cross-over design) 1h after onset of the dark period, and regained access to chow 30 min after injection (t=0). Food intake and locomotor activity were recorded every 15 min. Inhibition of NAcc A2a/D2 MSNs did not affect feeding behavior nor locomotor activity (n=13). Finally, 30 min after being placed in a novelty situation consisting of a clean cage with a metal grid covering the bottom, half of the rats received CNO and the other half saline. The novel situation increased latency to feeding (mean difference=22.11 min, SEM of difference=8.73: p<0.05, n=9 consisting of A2a+ and - rats), which tended to be decreased by CNO p=0.1, n=5 for saline, n=7 for CNO). In summary, either activation of D2/A2a MSNs in the NAcc or a novel situation led to delayed feeding onset in rats. A bigger group of rats is needed to confirm that inhibition of these cells can abolish the novelty-induced feeding latency.

P242

Dopamine Responses To The Taste Of Sodium Chloride Are Modulated By Different Need States In A Concentration-Dependent Manner.

Paula Bazzino, Max Loh, Mitchell Roitman
University of Illinois at Chicago, Chicago, IL, United States

Sodium appetite is an innate, natural behavior where sodium deficit promotes vigorous seeking and consumption of sources of sodium at concentrations that would otherwise be avoided. Multiple brain structures play a role in signaling sodium deficit and promoting sodium seeking and consumption. Some of these signals rapidly quiesce with exposure to sodium. We have previously shown that sodium depletion recruits phasic dopamine release in the nucleus accumbens to intra-oral infusions of a hypertonic sodium solution. As sodium consumption continues, the appetite is sated. However, it remains unknown whether dopamine responses in animals that have undergone sodium depletion quiesce with consummatory behavior of sodium chloride in a concentration-dependent manner. We made brief intra-oral infusions of different sodium chloride concentrations while measuring real time dopamine transients through in vivo fiber photometry in the nucleus accumbens lateral shell. Recordings were made when the same rats were in sodium replete and deplete states. Linear regression of the data showed significant differences in the y-intercept for each concentration of sodium in sodium deplete versus replete conditions – supporting past work that physiological state modulates a dopamine response to a sodium solution. In the deplete condition, slopes of the linear regression statistically differed – suggesting that the dopamine response was sensitive to post-ingestive feedback based on sodium concentration. Future work will assess whether the negative slope of dopamine release across trials is due to a loss of excitatory drive from depletion or the development of negative feedback from the accumulation of ingested sodium.

P243

Local Melanocortinergic Signaling In The Parabrachial Nuclei Modulates Ingestive Behaviors

Naima / S Dahir^{1,2}, Yanan Wu^{1,3}, Lilly Zygodic^{1,4}, Roger / D Cone^{1,2,3}

¹Life Sciences Institute, University of Michigan, Ann Arbor, MI, United States, ²Molecular and Integrative Physiology, University of Michigan, Ann Arbor, MI, United States, ³Cellular and Developmental Biology, University of Michigan, Ann Arbor, MI, United States, ⁴Michigan Engineering, University of Michigan, Ann Arbor, MI, United States

It is well-established that melanocortin receptors (MC3R and MC4R) and their ligands, AgRP and POMC-derived MSH peptides, regulate feeding behavior. While the hypothalamic expression of MC3R and MC4R has been long recognized to regulate energy homeostasis, we have characterized the expression and function of the MC3R and MC4R in the parabrachial nucleus (PB). Neuronal markers like CGRP neurons are known to play a role in feeding and adaptive behaviors within the PB; however, markers for neurons that integrate the complex inputs that the PB receives are unknown – particularly those that respond to nonaversive ingestive signals. We have documented that the MC3R and MC4R are expressed in non-overlapping neurons in the PB, with MC4R distributed across nuclei in the PB, whereas MC3R is almost exclusively in the lateral medial part of the PB. Using DREADDs and pharmacological approaches, we found that activating MC4R in the PB profoundly suppresses food and fluid intake, impairs fast-refeeding hyperphagia, and induces anxiety-associated behaviors. Importantly, the MC3R neurons represent a novel population in the PB as they contradict the overall role of the PB in inhibiting feeding. Pharmacological activation of MC3R in the PB directs mice to consume more food. Of interest, the global deletion of *Mc3r* in mice increases stress and anxiety-induced anorexia, whereas the global deletion of *Mc4r* leads to hyperphagia and obesity. We are currently elucidating if or how these two receptors in the PB coordinate their function to influence ingestive behaviors. The findings from these studies will provide an in-depth understanding of the role of melanocortinergic signaling in regulating sensory-driven ingestive behaviors by the PB and contribute to our understanding of intra-PB microcircuitry.

P244

Endocannabinoid Signaling To Astrocytes In The Hypothalamus Modulates Feeding Behavior And Energy Metabolism

Daniela Herrera Moro Chao¹, Xian Sun¹, Carmen Nanclares¹, Dana Deters¹, Maria Razzoli², Mary Brown¹, Alessandro Bartolomucci², Paulo Kofuji¹, Alfonso Araque¹

¹Department of Neuroscience, University of Minnesota, Minneapolis, MN, United States, ²Department of Integrative Biology and Physiology, University of Minnesota, Minneapolis, MN, United States

The brain controls energy homeostasis by fine tuning feeding and energy expenditure to nutrient availability. Disruption of this regulation results in obesity and associated metabolic pathologies. In particular, the lateral hypothalamus (LH) mediates autonomic metabolic regulation and motivational processes underlying feeding behavior. Over the last decades, evidence has shown that hypothalamic circuits are highly vulnerable to obesogenic diets and that diet-induced obesity (DIO) modifies astrocyte physiology, which contributes to local hypothalamic inflammation. The endocannabinoid (eCB) system participates in the pathophysiology of obesity, partly through the activation of type 1 eCB receptors (CB1Rs) in the brain and peripheral organs. Importantly, eCBs modulate synaptic function through the activation of astrocytic CB1Rs. By combining Ca²⁺ imaging selectively in astrocytes and in vivo metabolic profiling, we explored the contribution of astrocyte eCB signaling in the LH in the development of DIO. We show that astrocytic CB1R contributes to DIO-induced astrocyte hyperactivity and reactivity in the hypothalamus. Additionally, in vivo phenotyping after astrocyte CB1R KO in the LH shows increased food intake and body weight and decreased insulin sensitivity in lean and obese mice. In conclusion, our findings suggest that astrocyte eCB signalling plays a crucial role in obesity-associated functional changes in hypothalamic astrocytes and contributes to disbalances in systemic glucose metabolism and energy homeostasis associated with the development of DIO.

P245

Reduced Liver Mitochondrial Energy Homeostasis Impairs Food Intake Regulation Following Oral Preloads And Fasting

Michael E. Ponte¹, John C. Prom¹, Caroline E. Geisler², Matthew R. Hayes², E. Matthew Morris¹

¹Dept. of Cell Biology & Physiology, University of Kansas Medical Center, Kansas City, KS, United States, ²Dept. of Psychiatry, University of Pennsylvania, Philadelphia, PA, United States

Increased acute food intake via inhibition of liver oxidative metabolism has been observed for decades. However, many of these experiments did not target the liver specifically, confounding the interpretation of the outcomes. We have observed that male mice with reduced liver mitochondrial fatty acid oxidation and respiratory capacity due to hepatocyte-specific PGC1a heterozygosity (LPGC1a), gain more weight during short-term high-fat diet feeding than wildtype littermates in part through increased food intake and meal size. To assess the impact of liver energy metabolism changes on acute food intake regulation in male LPGC1a mice, we monitored food intake following mixed and individual nutrient oral preloads, and after an 18 hr fast. LPGC1a mice had significantly reduced dose-dependent food intake inhibition following Ensure oral preloads, as well as, reduced food intake inhibition during oral preloads of individual macronutrients compared to wildtype littermates. This impairment in acute food intake inhibition was characterized by increased meal size and duration, with no difference observed in number of meals. Further, IP delivery of satiation receptor antagonists (i.e., 5HTR3 – Ondanestron, CCK1R – Lorglumide, GLP1R – Exendin-9) failed to increase food intake following an Ensure oral preload to the same level as wildtype. Finally, the fasting-induced refeeding response was twice as robust in the LPGC1a mice compared to wildtype. This was due to greater LPGC1a fasting-induced 30-minute food intake with greater meal size and was not blocked by exogenous CCK-8 delivery. Together these results support the potential of the liver to serve as an energy sensor in the interoceptive regulation of food intake. Funding: P20GM144269 (EMM), K01DK112967 (EMM)

P246

Vagus Mediated Satiety Is Impaired Within 4 Weeks Of High Fat Feeding In Rats

Arashdeep Singh^{1,2}, Molly McDougle^{1,4}, Claire de La Serre³, Guillaume de Lartigue^{1,2}

¹Monell Chemical Senses Center, Philadelphia, PA, United States, ²University of Pennsylvania, Philadelphia, PA, United States, ³Colorado State University, Fort Collins, CO, United States, ⁴Florida State University, Tallahassee, FL, United States

Vagal sensory neurons are a crucial part of the nutrient-sensing machinery that mediates satiation. In diet-induced obesity, vagal fibers are reorganized in the hindbrain, and experimentally disrupting vagal signaling from the gut promotes overeating and weight gain. The extent to which vagal mediated satiation is impaired in response to a high-fat diet (HFD), the time course of vagal remodeling, and whether vagal sensory fibers that signal meal-related information are reorganized in the hindbrain remains unclear. **Methods:** To target gut-innervating nodose ganglia neurons (NG^{gut}) we injected retrograde Cre virus into the stomach and duodenum of chow-fed age-matched rats. To enable chemogenetic stimulation of NG^{gut} neurons, we bilaterally injected Cre-dependent hM3Dq virus in the NG of these rats. Rats with confirmed CNO-induced vagal-mediated satiation, were placed in a BioDAQ feeding system and maintained on either chow or HFD for 8 weeks. At 0, 4 and 8 weeks, we measured food intake in response to CNO and saline for each animal. To assess the time course of NG^{gut} remodeling, separate rats received bilateral NG injection of Cre-dependent red reporter and brains were collected at 0, 1, 2, 3, 4, and 8 weeks of HFD. **Results:** Chemogenetic stimulation of NG^{gut} inhibits food intake at all timepoints in rats maintained on chow. However, CNO-induced vagal satiety was severely blunted after 4 and 8 weeks of HFD in rats previously found to reduce food intake in response to CNO while on chow. We are processing the brain to assess the timecourse of vagal remodeling. **Conclusion:** Vagal induced satiety is impaired within 4 weeks of HFD, even when bypassing impaired vagal sensing of meal related signals in the gut.

P247

Development Of A Standardized Algorithm To Match Nutrient Composition Across Foods, Meals, And Diets

Monica L Ahrens¹, Zachary Hutelin^{2, 3}, Mary Elizabeth Baugh^{3, 4}, Alexandra G DiFeliceantonio^{3, 4, 5}

¹Center for Biostatistics and Health Data Science, Department of Statistics, Virginia Tech, Roanoke, VA, United States, ²Graduate Program in Translational Biology, Medicine, and Health, Virginia Tech, Blacksburg, VA, United States, ³Fralin Biomedical Research Institute at VTC, Roanoke, VA, United States, ⁴Center for Health Behaviors Research at Fralin Biomedical Research Institute at VTC, Roanoke, VA, United States, ⁵Department of Human Nutrition, Foods, and Exercise, Virginia Tech, Blacksburg, VA, United States

Matching nutrient composition across experimental group foods, diets, and meals is a common need in controlled feeding and nutrition studies. Historically, researchers have used a “brute force” method to develop research meals and diets matched on nutrients of interest, which can be a tedious process and is typically limited in number of matched nutrients. Recently, we developed an algorithm to match sets of foods or meals on any number of macro- and micro-nutrients, including fiber and water content. The algorithm uses information provided by the user, such as food nutrition information, group designation, the smallest possible increment of a food, the largest amount for each food able to give to a participant, and then processes all possible combinations of foods and food amounts in each identified group to yield matched results. We applied this algorithm to an ongoing study examining the effect of food processing on human metabolism, in which two meals with the same nutrient composition, but one comprised of entirely ultra-processed foods and one entirely of minimally processed foods, were compared. Our algorithm was able to develop 300-calorie ultra-processed and minimally processed meals that were matched on weight, energy, total carbohydrates, total fats, total proteins, available carbohydrates, glycemic index, glycemic load, total dietary fiber, sodium, and water all with

9:30 - 10:00 AM	Riverwalk A
Coffee Break	
10:30 - 12:10 PM	Ballroom III
Symposium 2: Animal Models of Anorexia Nervosa: Identifying Vulnerabilities, Consequences and Therapeutics	

Chair(s): Tim Moran

P2
10:30

Targeting Cognitive Function To Treat Anorexia Nervosa & Insights Into The Effects Of Psilocybin In Animal Models

Kyna Conn^{1,2}, Felicia Reed^{1,2}, Laura K Milton^{1,2}, Kaixin Huang^{1,2}, Alexander Reichenbach^{1,2}, Claire J Foldi^{1,2}

¹Monash Biomedicine Discovery Institute, Clayton, Australia, ²Monash University, Clayton, Australia

Anorexia nervosa (AN) has one of the highest mortality rates of any psychiatric disorder and less than 50% of patients ever recover. Despite this, there are currently no effective medicinal treatments. Psilocybin is currently being explored as a novel therapeutic for AN, and is proposed to act by “breaking down” inflexible patterns of thought and behaviour. To investigate the biological determinants of pathological weight loss, we use a well-established rodent model called activity-based anorexia (ABA), in which unlimited access to a running wheel paired with time-limited access to food precipitates voluntary hyperactivity, voluntary starvation, and rapid body weight loss. In this presentation, I will describe studies investigating the effects of psilocybin on anorectic behaviour in ABA rats and on a range of cognitive behaviours using novel open-source home-cage operant testing devices (the Feeding Experimental Device 3; FED3) across a range of tasks. I will show how these effects are mediated by signalling through specific serotonin receptor subtypes and the direct effects of psilocybin on dopamine release in response to food rewards and under contexts of uncertainty. Taken together, these findings provide initial support for the therapeutic potential of psilocybin for treating cognitive symptoms of AN and highlight a need to understand the mechanistic bases of psychedelics beyond a focus on serotonin system function. These studies were supported by the National Health and Medical Research Council of Australia (GNT2011334).

P1
10:55

Sub-Anesthetic Dose Of Ketamine And Ketogenic Diet Reduce Vulnerability Of Mice To Anorexia-Like Behavior By Evoking Synaptic Plasticity

Chiye Aoki, Yiru Dong, Yi-Wen Chen, Rose Temizer, Jennifer Li, Bridget Xu, Cassandra Carrasco
CNS, New York University, New York, NY, United States

Activity-based anorexia (ABA) is an animal model that captures key maladaptive behaviors of anorexia nervosa – hunger-evoked hyperactivity, voluntary food restriction, elevated anxiety, leading to severe weight loss. A single sub-anesthetic dose of intraperitoneal ketamine was shown to ameliorate severity of the maladaptive behaviors of adolescent female mice acutely and > 15 days post-injection (DOI: 10.1002/eat.22937). Ultrastructural analysis of the medial prefrontal cortex (mPFC) of ketamine-treated animals with improved behaviors revealed increased levels of NMDA and AMPA-type glutamate receptors and of drebrin, a protein known to promote activity-dependent rapid trafficking of NMDA receptors to the synaptic membrane. These changes occurred within spine heads, at sites very near (<1 µm) but clearly still removed from the synaptic membrane. Such locations can support rapid changes in synaptic strength without increasing steady-state excitability. Correlation analyses of these synaptic molecules with anorexia-like behavior indicate that ketamine-induced synaptic plasticity of ABA mice is specific for neural pathways originating in the mPFC that promote feeding and suppress hyperactivity. Unfortunately, ketamine is less efficacious for ABA mice in adulthood (N=13). Prompted by positive outcomes of studies (N=6) that combined ketogenic diet (KG, high fat/low carb) with ketamine to treat persons with anorexia nervosa, we’ve tested the effect of KG, alone, on adult ABA mice (N=31). Indeed, KG is highly efficacious in reducing hunger-evoked hyperactivity and weight loss, thereby improving survival. We are testing the hypothesis that this may be through BDNF (Brain Derived Neurotrophic Factor)-mediated synaptic plasticity in hippocampus and brain regions connected to it.

P3
11:20

Role Of The Ghrelin/Leap2 Balance In Abnormal Eating Behavior In Anorexia Nervosa (Supported By The Ssib International Foundational Fund Given In Memory Of Drs. Jacques Le Magnen (France), Anton Steffens (The Netherlands), Jacob Steiner (Israel), Steven Cooper (The United Kingdom))

Virginie TOLLE

Institute of Psychiatry and Neuroscience of Paris, INSERM UMR1266, Paris, France

Anorexia nervosa (AN) is a severe eating disorder with life-threatening consequences that mainly affects young women. AN is characterized by self food-restriction leading to severe weight loss and harmful undernutrition. While the etiology of this disorder remains largely unknown, AN is now recognized as a disorder of brain reward processes abnormalities. Furthermore, recent large-scale genetic data allowed to re-conceptualize AN as a disorder with both psychiatric and metabolic origins. However, the exact underlying mechanisms linking metabolic sensors and AN symptoms are poorly understood. Amongst metabolic sensors involved in brain circuits controlling energy homeostasis and reward encoding, ghrelin is one of the most characterized. Ghrelin, is a peptide hormone, produced mainly in the stomach, acting on the GHSR (Growth hormone Secretagogue Receptor) that promotes food intake and stimulates food related motivated behaviors. Its plasma concentrations are increased in anticipation of meals and is elevated in undernourished AN patients, despite reduced food intake. LEAP2 (Liver Enzyme Expressing Anti-microbial Peptide), produced mainly in the liver and intestine, has been identified as an antagonist of ghrelin at the GHS-R, inhibiting ghrelin-induced food intake. Our objective is to investigate how these two antagonistic peptides are modulated by the undernutrition state in physiological and pathological eating and how they participate in processes underlying abnormal feeding behavior in AN. To address this question, I will present a translational approach *i)* in a mouse model of chronic calorie restriction that mimics the main metabolic features of AN and *ii)* in patients with AN in a longitudinal follow-up study under both undernourished and refed states.

Identifying Systems Regulating The Effects Of Stress On Eating Behavior In Mice

Lori Zeltser

Columbia University Irving Medical Center, New York, NY, United States

Stress almost always alters eating behavior, particularly in the context of high calorie foods with low nutritional value. However, the direction of the response is inconsistent, with consumption increased in some individuals (called emotional eating or stress eating) but decreased in others. The determinants of these responses to stress are unknown. There is strong evidence of genetic contributions to disordered eating behaviors, but findings with specific gene variants are inconsistent. We developed a mouse model that reliably elicits stress-related increases in caloric intake in wild-type C57BL/6J males and females. We are using this paradigm to explore how genetic factors influence this behavior in mice carrying a common gene variant, *Brain derived neurotrophic factor*-Val66Met (*hBDNF*-Met), which has been associated with increased risk of anorexia nervosa in some cohorts.

Oral Session 4: Gutsy Brain: Integration of Peripheral and Central Signals

Chair(s): Will de Lartigue

10:30

Neuropod Cells In The Duodenal Epithelium Drive Food Reward

Laura E. Rupprecht, Carlos Puerto, Diego V. Bohorquez
Duke University, Durham, NC, United States

Guided by gut sensory stimuli, animals prefer foods rich in fats. In the intestinal epithelium, cholecystokinin (CCK)-expressing neuropod cells synapse with vagal neurons to communicate the presence of a nutrient in milliseconds. Given that gut-innervating vagal neurons are sufficient to drive reward behaviors and that nutrients do not contact the vagus, we hypothesized that neuropod cells are essential for the pleasure of nutrients in the gut. To test this, we used the real-time place preference test in which a mouse's location in a cage will trigger an intestinal nutrient infusion or an optogenetic light pulse. To optogenetically stimulate neuropod cells, we developed a flexible fiberoptic cable for implant in the lumen of the intestine. To test if neuropod cells are sufficient for reward, we implanted the fiber in mice expressing an excitatory opsin in CCK cells (CckCre-ChR2). CckCre-ChR2, but not littermate control, mice had a robust preference for optostimulation, indicating these cells drive reward from the gut. We then repeated the experiment in wild-type mice equipped with duodenal catheters receiving intestinal nutrient infusion based on real-time location. There was a strong preference for intestinal fat, but not for equicaloric sugar. Neuropod cells release CCK and glutamate in response to nutrients. Blocking CCK-A receptors with devazepide had no impact on fat preference. However, intraduodenally inhibiting ionotropic glutamate receptors with kynurenic acid blocked the preference for intestinal fat. Fat preference was also ablated by conditional knockout of the vesicular glutamate transporter 1 in CCK cells. Therefore, glutamate from neuropod cells in the proximal duodenum guide the choice for fats that evoke a pleasurable feeling.

10:45

Reward Learning For Sugars With Varying Rates Of Absorption And Utilization

Mary Elizabeth Bugh^{1,2}, Amber Burns^{1,2,3}, Abigail Valle⁴, Rhianna Sullivan⁵, Monica Ahrens⁶, Alexandra DiFeliceantonio^{1,2}

¹Fralin Biomedical Research Institute at VTC, Roanoke, VA, United States, ²Center for Health Behaviors Research at Fralin Biomedical Research Institute at VTC, Roanoke, VA, United States, ³Translational Biology, Medicine, and Health, Fralin Biomedical Research Institute at VTC, Roanoke, VA, United States, ⁴Department of Biological Sciences, Virginia Tech, Blacksburg, VA, United States, ⁵School of Neuroscience, Virginia Tech, Blacksburg, VA, United States, ⁶Center for Biostatistics and Health Data Science, Department of Statistics, Blacksburg, VA, United States

In addition to hyperpalatable qualities (e.g., high fat and sugar content), ultra-processed foods are characterized by industrial processing, which reduces fiber content and increases bioavailability of calories. Prior work in rodents and humans highlights the importance of post-ingestive glucose and sucrose sensing and utilization in driving learned preferences for sugars, but whether the speed at which sugars are absorbed and utilized modulates their reinforcement potential is unknown. Our aim is to assess brain response and behavioral preference for sugars with varying rates of absorption and utilization. In this ongoing randomized, crossover, flavor-nutrient conditioning study, participants aged 18-45 y (target: n=64) consume sweet, novelty flavored drinks containing no calories (sucralose; CS-), 75 calories of sucrose (CS+Fast), and 75 calories of maltodextrin [glucose] + fiber (CS+Slow) 6 times each. Post-test ratings of wanting and pre-to-post changes in rated liking are assessed as behavioral preference measures; post-test brain response (fMRI) to each flavor (without calories) is assessed. Preliminary analyses using linear mixed effects models (n=7) suggest differences across conditions in change in liking ratings, with a trend toward lower change in liking for CS+Slow compared with CS- ($\beta = -10.19$, $p = 0.06$). Preliminary brain analyses revealed increased activity in the right posterior insula in response to CS+Slow vs. CS- ($[38\ 2\ -12]$, $p < 0.001$ uncorr, $k = 42$), which did not survive multiple comparisons correction. Data collection is ongoing, and as outcomes of flavor-nutrient conditioning are subtle measurements in humans, more participants are needed. This work is an important step in exploring whether food processing drives food reward and reinforcement.

11:00

Gut-Derived Vagus Nerve Signaling Promotes Memory Function

Lea Decarie-Spain¹, Logan Tierno Lauer¹, Cornelia F Richter², Cindy Gu¹, Alicia Kao¹, Arun Ahuja¹, Alice Waldow¹, Xudong Wang³, Jean-Phillippe Krieger^{2,4}, Scott Kanoski¹

¹University of Southern California, Los Angeles, CA, United States, ²University of Zurich-Vetsuisse, Zurich, Switzerland,

³University of Wisconsin-Madison, Madison, WI, United States, ⁴University of Gothenberg, Gothenberg, Sweden

Gut-derived vagus nerve signaling promotes meal termination, yet emerging findings support an additional role in higher-order cognitive processes. Our group identified a multi-synaptic pathway connecting gut-derived vagal afferents to the

hippocampus, and further that subdiaphragmatic vagal afferent ablation impairs hippocampal-dependent memory. Whether these findings are relevant to humans is poorly understood. Further, it is unknown whether impaired hippocampal function associated with blunted gut vagal signaling can be reversed with vagus nerve stimulation (VNS). Addressing these gaps, we first used longitudinal data from the Swedish National Patient Registry to compare hazard ratios (HR) of dementia diagnosis between individuals who underwent a vagotomy versus age-matched healthy controls, with sex and age as confounding factors. Vagotomy was associated with an increased risk for dementia later in life (HR: 3.401) and this was driven by truncal (HR: 4.895) and not selective (HR: 2.543) vagotomy. Next, to identify whether memory impairments associated with impaired vagal signaling are reversible, male rats were implanted with a sham or functional subdiaphragmatic VNS device and were fed either standard chow or a high-fat-high-sucrose diet (HFHS) for 5 weeks, with the latter diet being strongly associated with blunted gut-to-brain vagal signaling. Results revealed that HFHS sham rats were impaired in two tests of hippocampal-dependent contextual memory (novel object in context, meal place recognition), whereas VNS prevented the HFHS diet-induced memory deficits. These findings identify a potential role for gut-derived vagus nerve signaling in the etiology of human dementia, and further illuminate a potential therapeutic approach for diet-associated memory deficits.

11:15 **Associations Between Gut Transit Time And Satiety Differ In Individuals With Spinal Cord Injury Versus Controls (New Investigator Travel Awardee)**

Gary J. Farkas^{1,2}, Paige M. Cunningham^{3,4}, Alicia Snej¹, Il Joon Paik⁵, Mark S Nash^{1,2}, Barbara J. Rolls³

¹Department of Physical Medicine & Rehabilitation, University of Miami Miller School of Medicine, Miami, FL, United States, ²The Miami Project to Cure Paralysis, University of Miami Miller School of Medicine, Miami, FL, United States,

³Department of Nutritional Sciences, The Pennsylvania State University, University Park, PA, United States, ⁴Sensory Evaluation Center, Department of Food Science, The Pennsylvania State University, University Park, PA, United States,

⁵Division of Digestive Health and Liver Disease, Department of Medicine, Miami, FL, United States, ⁶Department of Public Health Sciences, The Pennsylvania State University College of Medicine, Hershey, PA, United States

Spinal cord injury (SCI) prompts neurogenic obesity, and subsequent gut dysregulation may impair satiety. We examined the association between gut transit time and satiety in men with and without SCI. We hypothesize that delayed gastric emptying after SCI is associated with altered hunger and fullness. After an 8-hr fast, 16 men with SCI (Age: 42±15 y, BMI: 26±5 kg/m², 50% paraplegia) and 16 controls (Age: 42±14 y, BMI: 26±5 kg/m²) consumed a standard meal (255 kcal), followed by ingestion of a SmartPill capsule (Medtronic), measuring whole and regional gut motility. Visual analog scales (VAS) were administered 60 min before and every 30 min for 120 min after the meal. We calculated the area under the curve using all postprandial time points for hunger, fullness, and prospective food consumption (PFC). Multivariate linear regression models assessed associations between VAS and gut motility. Demographics did not differ between groups (p>0.05). Small bowel (SBTT), upper gut, colonic, and whole gut transit time were lower in SCI than controls (all p<0.03). Adjusting for group, each increase/hr in SBTT and gastric emptying was associated with greater fullness (β=1298.8, p=0.054) and less hunger (β=-1671.2, p=0.074), respectively. Men with SCI reported more hunger (β=-8626.9) and less fullness (β=8682.1) and PFC (β=-7925.7) than controls for the same SBTT (all, p≤0.04). Reported hunger showed a stronger positive association with SBTT (β=1653.9), while reported fullness showed a weaker negative association (β=-1793.2) in men with SCI than controls (both p<0.05). Gut dysmotility after SCI may mediate altered hunger and fullness sensations by disrupting gut-brain signaling, particularly from the small bowel, potentially contributing to overeating and neurogenic obesity.

11:30 **Comparison Of Glial Fibrillary Acidic Protein And S100B To Identify Astrocytes And Impacts Of Sex And High Fat Diet**

Beenhwa G. Lee, Pooja Menon, Charlotte Schultz, Raluca Bugescu, Gina M. Leininger
Michigan State University, East Lansing, MI, United States

Glial fibrillary acidic protein (GFAP) is commonly used as a marker of astrocytes and mice fed high fat diet (HFD) exhibit increased GFAP immunoreactivity in astrocytes of the mediobasal hypothalamus. Yet, there is scant immunolabeling of GFAP in brains of chow-fed mice, despite the presence of abundant astrocytes. These findings underscore the need for a marker to visualize all astrocytes throughout the brain during normal physiology and exposure to diet-induced obesity, to permit study of how and where they contribute to energy balance. Here we immunofluorescence labeled GFAP and another protein expressed in astrocytes, S100B, in brain sections from chow- and HFD-fed female and male mice. We compared the number of labeled cells and fluorescence intensity in areas pertinent to control of ingestive behavior: the arcuate nucleus, lateral hypothalamic area, lateral preoptic area, and the periaqueductal gray. We found that S100B reliably labeled more cells than GFAP in each of these brain regions in chow and HFD-fed mice, and across females and males. Furthermore, HFD increased the number of S100B-labeled cells or their fluorescence (e.g. amount of expressed S100B) in all brain areas examined, while such change in GFAP labeling was only detected in the lateral preoptic area. Apart from a slight sex difference in the periaqueductal gray and the lateral preoptic area, S100B labeled equivalent numbers of astrocytes in female and male mice. Overall, these data suggest that S100B is superior to GFAP in visualizing astrocytes throughout the brain in both sexes and their response to HFD. This study will be a useful resource for researchers who want to identify and study astrocytes in response to diet and in other physiological contexts.

11:45 **Biased Agonism Of The Glp-1R By Ex-Phe1 Maintains Glycemic Control Without Nausea/Emesis Or Suppression Of Body Weight**

Caitlin Baumer-Harrison¹, Danya Aldaghma², Nancy Cham³, Minrong Ai⁴, Ricardo J Samms⁴, Robert P Doyle³, Tito Borner², Bart C De Jonghe², Matthew R Hayes¹

¹Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States,

²Department of Biobehavioral Health Sciences, School of Nursing, University of Pennsylvania, Philadelphia, PA, United States, ³Department of Chemistry, Syracuse University, Syracuse, NY, United States, ⁴Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN, United States

Glucagon-like peptide-1 receptor (GLP-1R) agonists enhance glycemic control, induce hypophagia, and promote weight loss. However, they produce nausea and emesis in a significant percentage of patients. Thus, there is a need to develop novel GLP-1R therapies to mitigate these side effects. Exendin-Phe1 (Ex-Phe1), modified from the GLP-1R agonist Ex-4 by

a single amino acid substitution (His1 → Phe1), is reported to induce biased agonism of the GLP-1R toward cAMP signaling with reduced β -arrestin recruitment. We hypothesized that Ex-Phe1 would maintain glycemic control without producing emesis in musk shrews (*Suncus murinus*). Hence, we examined glycemic control, feeding, and emesis following Ex-4 and Ex-Phe1 administration. Ex-4 and Ex-Phe1 similarly enhanced glucose tolerance compared to vehicle. Ex-Phe1 had modest effects on food intake and body weight and produced significantly fewer emetic episodes compared to Ex-4. Ex-4 and Ex-Phe1 induced c-Fos expression within the area postrema and nucleus of the solitary tract, regions involved in mediating the nausea and emetic side effects of GLP-1R agonism. Collectively, these results indicate that the biased actions of Ex-Phe1 towards cAMP without β -arrestin recruitment is sufficient for an incretin-mediated glycemic control, but putatively blunts the ability of the CNS GLP-1R⁺ cells to drive anorexia and weight loss, as well as unwanted adverse events (nausea/emesis). This study highlights the beneficial action of biased agonism of the GLP-1R for the treatment of type 2 diabetes and sheds light on the importance of understanding the requirement of β -arrestin recruitment in eliciting the suppression of food intake and illness-like behaviors from GLP-1R agonists.

12:00

Orexin Signaling Modulates Uncertainty-Driven Food-Seeking Behavior

Luis Luarte¹, Magdalena Figueroa¹, Carolina Sandoval¹, Jen Teske², Kevin Myers³, Claudio Perez¹

¹Neurobiology and Obesity (NBO) Laboratory, Department of Physiology, Faculty of Biological Sciences, Pontificia Universidad Católica de Chile, Santiago, Chile, ²School of Nutritional Sciences and Wellness, Graduate interdisciplinary programs in Physiological Sciences and Neuroscience at the University of Arizona, Tucson, AZ, United States, ³Department of Psychology and Neuroscience Program, Bucknell University, Lewisburg, PA, United States

Uncertainty in food access increases food-seeking and increases the risk of obesity, but the underlying mechanisms remain poorly understood. We propose that uncertainty alters food-seeking behavior via orexin receptor activity. Male (8 weeks) C57BL6 mice were used for all experiments. We modeled uncertainty in sustenance food (food required to fulfill caloric needs, SF) by using an unpredictable versus predictable pellet delivery (after pellet retrieval, the next pellet was delivered with a random or constant delay, n=8/group), after 8-weeks mice were tested in a sucrose demand task followed by RNAseq in hypothalamic samples. In another set of mice, we used a two-alternative forced choice task (2AFC) where mice were offered condensed milk with 100/100%, 100/50%, 50/25% probability of delivery and were injected with TCS-1102 (dual orexin receptor antagonist, 10 mg/kg) or vehicle (n=8, repeated measures). In these experiments, mice had access to enough calories to sustain their body weight. Compared to control animals, SF uncertainty decreased demand elasticity (M=-62.30%, SEM=9.40%, p<0.05) and RNA-Seq analysis showed increased orexin mRNA expression in the uncertainty condition (random-forest model, 68% accuracy, leave-one-out cross-validation). In the 2AFC task, TCS-1102 increased latency to obtain uncertain rewards (M=30.30%, SEM=16.66%, p<0.05) and reduced latency to obtain certain rewards (M=-23.80%, SEM=8.15%, p<0.05). Also, reinforcement-learning parameter fitting showed that TCS-1102 decreased selection of uncertain rewards (M=-10%, SEM=5.50%, p<0.05). Together, these data suggest that orexin activity mediates the increase in food-seeking when facing an uncertain environment.

12:15 - 1:00 PM	Ballroom III
NIAB Professional Development Event - Artificial Intelligence by Dr. Theja	

Lunch included for the first 45 new investigators (students, techs, postdocs) RSVP Required. Pinched on the River, Mediterranean. Register here: <https://docs.google.com/forms/d/e/1FAIpQLSdxM3a3c8ARatusIjVxnFtQ1mF6Fa1B1L2IISvQlfqHLXUGkA/viewform>

12:15 - 1:45 PM	On Own
Lunch	

12:30 - 1:30 PM	Illinois Boardroom
PHYSIOLOGY & BEHAVIOR EDITORIAL BOARD MEETING (INVITATION ONLY)	

1:45 - 2:45 PM	Ballroom I-II
MARS Lecture 2	

Chair(s): Carrie Ferrario

1:45

Cued Up For Rewards: How Do “Bells And Whistles” Alter Motivation For Risky Gambles?
Catharine A. Winstanley
UBC, Vancouver, BC, Canada

It has long been known that audiovisual cues, when paired repeatedly with appetitive outcomes like sugary rewards or liquids, can come to act as reinforcers in their own right due to the attribution of incentive salience. Electronic gambling machines and gaming apps make heavy use of these cues to signal rewarding events during play. We have shown that, in both rats and humans, presenting sound and light cues concurrent with reward delivery can increase preference for “high-risk, high-reward” options in laboratory-based gambling tasks. However, computational modeling using reinforcement learning algorithms suggest that cue-induced risky choice is not driven by enhanced learning from rewards, as we would expect if the cues were acting as conditioned reinforcers, but instead through impaired learning from penalties. Furthermore, analyses of data from nearly 700 rats suggest that even though the risk-promoting effect of the cues looks superficially similar across sex, cue-induced risky choice may operate via different cognitive processes in females vs males. Data from behavioral pharmacology studies and chemogenetic manipulations suggest reward-concurrent cues alter the recruitment of multiple neurotransmitter systems and brain regions in the decision-making process. Although daunting in its complexity, these studies also suggest a variety of approaches that may neutralize the deleterious effect of such cues on cognition.

2:45 - 4:45 PM	Ballroom I-II
NITA Symposium	

Chair(s): Mitch Roitman

2:45

Early Life Western Diet Exposure Impairs Vagus Nerve-Mediated Hippocampus Cholinergic Signaling (Randall R. Sakai New Investigator Travel Awardee) .A

Logan Tierno Lauer¹, Lea Decaire-Spain¹, Andrea N. Suarez¹, Anna M. Hayes¹, Molly E. Klug¹, Alicia E. Kao¹, Jessica J. Rae¹, Keshav S. Subramanian¹, Guillaume de Lartigue², Cindy Gu¹, Anna Nourbash¹, Kristen Donohue¹, Kevin Myers³, Scott E. Kanoski¹

¹University of Southern California, Los Angeles, CA, United States, ²Monell Chemical Sense Center, Philadelphia, PA, United States, ³Bucknell University, Philadelphia, PA, United States

Chronic exposure to a Western diet (WD) elicits hippocampal (HPC)-dependent memory impairment. One potential unexplored mechanism for these effects involves impaired vagus afferent nerve (VAN) signaling, as VAN signaling promotes HPC function, and WD consumption blunts the capacity of vagally-mediated gut signals to communicate to the brain. The medial septum (MS) is an anatomical relay between the brainstem and the HPC, and the MS extensively innervates the HPC with acetylcholine (ACh) releasing fibers. Thus, we hypothesized that VAN signaling engages the HPC via MS ACh release, and further, that impairments in this signaling pathway underlie WD-associated HPC dysfunction. Using *in vivo* fiber photometry and fluorescent ACh sensors (iAChSnFR), we demonstrate that HPC ACh binding is elevated immediately following consumption of a meal. Additional results revealed that these meal-induced elevations in HPC ACh binding were eliminated in animals who underwent a surgical subdiaphragmatic vagotomy (SDV), thus identifying a role for vagal signaling in mediating postprandial HPC ACh signaling. To explore how a WD affects this outcome, we recorded HPC ACh binding in animals chronically exposed to a WD during development while consuming a meal during adulthood. Results reveal that, similar to SDV rats, meal-induced elevations in HPC ACh binding were eliminated in the WD group. Further, Western blot analyses revealed comparable reductions in HPC protein expression of vesicular ACh transporter, an indicator of ACh HPC tone, in SDV and WD rats relative to controls. Collectively, our findings identify ACh signaling as a neural substrate for gut-originating VAN potentiation of HPC function, and that impairments in this signaling pathway may underlie WD-induced HPC dysfunction.

3:00

Differential Metabolic And Brain Responses To Ultra-Processed And Minimally Processed Foods. (Elsevier Physiology & Behavior New Investigator Travel Awardee)

Zach Hutelin^{1,2}, Monica Ahrens³, Mary Elizabeth Baugh², Bert Herald², Alexandra L. Hanlon³, Alexandra G DiFeliceantonio^{2,4}

¹Graduate Program in Translational Biology, Medicine, and Health, Virginia Tech, Blacksburg, VA, United States, ²Fralin Biomedical Research Institute, Virginia Tech, Roanoke, VA, United States, ³Center for Biostatistics and Health Data Science, Virginia Tech, Roanoke, VA, United States, ⁴Department of Human Nutrition, Foods, and Exercise, Virginia Tech, Blacksburg, VA, United States

The minimally processed diets of our ancestors have been rapidly replaced by ultra-processed foods (UPF), leading to poor diet becoming the leading risk factor for preventable death globally. Hence, there is a pressing need to identify factors driving the consumption of UPF over minimally processed alternatives. To understand if the degree of food processing affects post-ingestive metabolic signaling, 12 healthy weight adults aged 18-45 underwent two 4-hour whole room indirect calorimetry metabolic measurements with simultaneous blood draws. On separate days, while undergoing the metabolic measures, participants consumed either a UPF or MPF meal matched within ~1% of energy, weight, carbohydrates, fats, protein, dietary fiber, glycemic load, and glycemic index. Consumption of the UPF meal resulted in a significantly greater area under the curve for blood glucose response ($p=0.018$), whereas consumption of the MPF meal resulted in greater carbohydrate oxidation ($p<0.0005$). The same participants also performed a Becker-DeGroot-Marschak auction paradigm concomitant with functional magnetic resonance imaging (fMRI) using a picture set we previously developed containing 14 UPF and 14 MPF. Participants were willing to pay more for MPF than UPF ($p=0.03$). Importantly, there was no difference between UPF and MPF in estimated price ($p=0.84$). Next, we investigated BOLD response to food picture viewing that was modulated by willingness to pay (WTP) for each picture. This revealed that WTP modulated brain response to MPF, but not UPF, in the fusiform cortex (near fusiform food area; $[-32 -56 -16]$, $pFWE<0.005$, $T=6.06$, $k=1748$). This suggests that value representation of UPF is altered compared to MPF, which may be an important factor driving the overconsumption of UPF.

3:15

No Association Between Peripheral Glucose Control And Central Insulin Sensitivity Or Cognition In Youth With Overweight/Obesity (George H. Collier New Investigator Travel Awardee)

Jade Quillian¹, Tuki Attuquayfio¹, Justin Sung¹, Tiffany Ko¹, Xue Davis¹, Kaitlin Maciejewski¹, Fangyong Li¹, Nicola Santoro¹, Stephanie Kullman², Hubert Preissl², Filip Morys³, Antonietta Canna³, Alain Dagher³, Sonia Caprio¹, Dana Small^{1,3}

¹Yale University, New Haven, CT, United States, ²University of Tuebingen, Tuebingen, Germany, ³McGill University, Montreal, QC, Canada

It is now well established that type 2 diabetes (T2D) is associated with cognitive impairment; however, adiposity is often not accounted for, and studies are conducted in older populations with co-morbid conditions that may affect cognition. Here we evaluated 67 youth with overweight/obesity (OW/OB) for anthropomorphic and metabolic measures, abdominal and hepatic adiposity, comprehensive cognitive testing, and the effects of intranasal insulin on working memory and on resting state brain activity and connectivity. Oral glucose tolerance tests diagnosed 22 participants with impaired and 45 with normal glucose tolerance (IGT/NGT). IGT and NGT groups did not differ in age, sex, race, IQ, or BMI; however, in IGT vs. NGT the visceral to subcutaneous fat ratio was higher and deep to superficial subcutaneous fat ratio trended as lower. These variables were therefore used as covariates in further analyses. Group (IGT vs. NGT) had no impact on any cognitive measure, nor on the effect of intranasal insulin (INI) on resting state brain activity. We did identify an association between the impact of INI on working memory and on caudate to premotor cortex connectivity, suggesting that INI influences working memory via this circuit independently of peripheral glucose control. By contrast, exploratory analyses revealed inverse associations between adiposity and working memory, visual recognition memory, verbal comprehension, and visuospatial processing. Results provide evidence that the association between T2D and cognitive impairment is driven by adiposity or co-morbid conditions associated with chronically impaired glucose tolerance.

3:30

Identification Of An Appetitive Engram In The Hippocampus That Controls Food Intake (Elsevier Appetite New Investigator Travel Awardee)

Mingxin Yang^{1,2}, Arashdeep Singh^{1,2}, Molly McDougle^{1,3}, Lea Decarie-Spain⁴, Scott Kanoski⁴, Guillaume de Lartigue^{1,2}

¹University of Pennsylvania, Philadelphia, PA, United States, ²Monell Chemical Senses Center, Philadelphia, PA, United States, ³Florida State University, Tallahassee, FL, United States, ⁴University of Southern California, Los Angeles, CA, United States

We set out to assess whether appetitive memory influences food intake. Significant progress has been made in locating the physical memory trace within the brain (engram), for aversive and social stimuli. Yet an appetitive engram has not been defined. **Methods:** The criteria to locate an engram are the ability to observe, erase and artificially express it in the brain. We

employed the Fos^{TRAP} mouse model to permanently tag activated dorsal hippocampal (dHPC) neurons to observe neural ensembles in response to appetitive stimuli (intragastric fat or sugar). We utilized viral-mediated neuronal ablation, and chemogenetic constructs in the dHPC of FosTRAP mice combined with memory tasks to assess the ability of dHPC neurons to erase or retrieve food location memory to fat or sugar. Intake of fat and sugar was monitored by lickometer while manipulating dHPC engrams. **Results:** We identified spatially segregated fat and sugar responsive dHPC populations. Ablation of sugar-responsive dHPC neurons erases sugar, but not fat, location memory. Ablation of fat-responsive dHPC neurons only impairs fat location memory. Stimulation of sugar-responsive neurons improve sugar memory retrieval as shown by increased context-specific memory for sugar location. We also found that stimulation of these appetitive engrams increased nutrient-specific intake, while their ablation inhibited nutrient-specific consumption. **Conclusion:** We identified novel populations of dHPC neurons that are necessary and sufficient for appetitive memory. We find that appetitive engram influence decisions about where to locate food, what to eat, and how much to consume. Collectively, these findings uncover a neural basis for the exquisite specificity in processing nutrient signals that shape dietary choices.

3:45

Early Developmental Perturbations To Fluid Homeostasis Impact The Organization Of Neuronal Feeding Circuits With Context-Specific Changes In Ingestive Behavior (New Investigator Travel Awardee)

Serena R. Sweet^{1,2}, Jessie B. Zimmermann¹, Jessica E. Biddinger^{1,2}, Gina L. Yu¹, Payam A. Fathi¹, Michelle N. Bedenbaugh^{1,2}, Richard B. Simerly^{1,2}

¹Vanderbilt University Department of Molecular Physiology & Biophysics, Nashville, TN, United States, ²Vanderbilt Center for Addiction Research, Nashville, TN, United States

Drinking and feeding are coordinated homeostatic events, but our understanding of the development of their converging hypothalamic neural circuits remains rudimentary. Many environmental factors influence formation of neural circuits during the early postnatal period, and agouti-related peptide (AgRP) neurons respond to nutritional cues during a critical period of development to reach downstream targets. The paraventricular nucleus of the hypothalamus (PVH) receives inputs from AgRP neurons and the median preoptic nucleus (MePO) to regulate energy and fluid homeostasis, respectively, representing a possible node of neural integration. We used *TRAP2;Ai14* mice to visualize neurons in the PVH responding to water deprivation (Thirst-TRAP) together with Fos activated by fasting/refeeding (HungerFos). DiI axonal labeling shows MePO projections reach the PVH by P8, preceding innervation by AgRP neurons. Fos-labeling established neurons in the MePO respond to hypertonic saline (HS) by P8, while PVH neurons respond at a peak in the second postnatal week. We then tested if perturbations to fluid homeostasis in neonatal mice alter formation of AgRP inputs to the PVH. Adult male mice exposed to HS treatment daily from postnatal day (P)5 to P15 (HS^{PN}) displayed significantly increased densities of AgRP axons in the MePO and PVH, compared to controls. Moreover, adult HS^{PN} mice displayed significantly greater water intake, but not food intake, in response to high fat diet, and showed blunted feeding and no changes to water intake after rehydration following a dehydration-anorexia challenge. Together, these results suggest development of feeding circuits is impacted by early perturbations to fluid homeostasis, with context-specific consequences for ingestive behavior.

4:00

Ventral Tegmental Area Oxytocin Receptor-Expressing Neurons Suppress Chow Intake In Mice (New Investigator Travel Awardee)

Patience E. Moseley, Lisa R. Anderson, Daniel O. Campos, Diana L. Williams
Florida State University, Tallahassee, FL, United States

Pharmacologic treatment with oxytocin (OXT) suppresses food intake in multiple species. Ventral tegmental area (VTA) OXT receptors (OXTR) may play a role because intra-VTA OXT suppresses intake and motivation for food. The OXTR is an excitatory receptor, therefore, we hypothesized that chemogenetic activation of VTA OXtr neurons suppresses food intake. In a preliminary study, male and female OXtrCre mice received bilateral intra-VTA injections of AAV for Cre-inducible hM3Dq (n=3M, 3F) or mCherry (n=1M, 1F). Mice were housed in the BioDAQ system to continuously monitor chow intake. After recovery, they received intraperitoneal (IP) injections of either CNO or vehicle, in counterbalanced order, 20 minutes before dark onset. Compared with vehicle, CNO suppressed chow intake in the hM3Dq mice from 4-6 h after dark onset (p<0.05). Tracing with an AAV for Cre-inducible synaptophysin-mCherry identified the nucleus accumbens (NAc) as a target of dense innervation by VTA OXtr neurons. Therefore, we hypothesized that activation of VTA OXtr neurons projecting to NAc mediate intake suppression. To test this, we induced hM3Dq expression only in VTA OXtr neurons that project to NAc by bilaterally injecting rgAAV for Cre-inducible Flp into NAc and AAV for Flp-inducible hM3Dq (n = 7M, 7F) or control mCherry (n = 3M, 2F) into the VTA of male and female OXtrCre mice. The experiment proceeded as described above, and here, CNO significantly reduced dark phase chow intake in hM3Dq mice by 18-28% at timepoints from 4-12 h (p<0.05). There were no apparent sex differences. Taken together, our results suggest that VTA OXtr neurons, particularly those projecting to NAc, control food intake. We are currently assessing whether this may involve suppression of motivation for food.

4:15

Bmi Moderates The Relationship Between Dopamine Synthesis And Behavioral Inhibition^Â (New Investigator Travel Awardee)

Afroditi Papantoni¹, Valerie L. Darcey², Kyle S. Burger¹

¹University of North Carolina, Chapel Hill, NC, United States, ²NIDDK/NIH, Bethesda, MD, United States

Dopamine's role in inhibitory control is well established, e.g., clinical populations suffering from reduced dopamine function show poor response inhibition. Further, inhibitory control is inversely related to obesity, where individuals with elevated BMI perform worse on inhibitory control tasks. Given that adiposity has been linked to increased dopamine tone, we sought to examine how BMI affects the relationship between dopamine and response inhibition. Healthy adults (n=50, 60% female, age=24±5 years, BMI=25.1±3.9 kg/m²) completed a neuromelanin-sensitive MRI scan which has been validated as a non-invasive, proxy measure of dopamine synthesis (DA) in neurons of the substantia nigra pars compacta (SNc); a region rich in dopamine that projects to brain regions associated with behavioral control. Participants also completed a stop signal task where stop-signal reaction time (SSRT) measures behavioral inhibition. We observed that DA in SNc was positively related to BMI (β=1.79, p=0.004), and showed evidence of a negative quadratic relationship (β=-0.03, p=0.005). Specifically, at low/moderate BMI levels DA was positively related to BMI, but at high BMI levels, DA had an

4:30

inverse relation with BMI. BMI also moderated the relationship between response inhibition and DA where subjects with high BMI had longer SSRT (poorer response inhibition) independent of DA, whereas for those with low/moderate BMI, greater DA was related to shorter SSRT (better response inhibition; $\beta=1.36$, $p=0.057$). These findings provide evidence that an elevated BMI may diminish dopamine's ability to regulate inhibitory control. This may be due to overeating highly rewarding foods that repeatedly engage dopaminergic systems, akin to the allostatic load model of compulsive behavior.

The Impact Of High-Energy Diet And Polygenic Obesity On The Dopamine Response To Cues Predicting Food Reward In Female Rats (New Investigator Travel Awardee)

Greta Lommi, Lorenz Klein, Thomas A. Lutz, Christina Neuner Boyle
Institute of Veterinary Physiology, University of Zurich, Zurich, Switzerland

The mesolimbic dopamine system is a crucial neural pathway which, through dopamine (DA) release from ventral tegmental area (VTA) neurons to the nucleus accumbens (NAc), regulates reward processing and motivation. This system influences behaviors like feeding and maternal care. However, disruptions due to dietary factors, especially palatable foods and obesity, can alter dopamine release and behavior. In this study, a polygenic rat model was used to explore the mesolimbic DA system's response to high-energy (HE) diets in obesity-prone (DIO) and obesity-resistant (DR) female rats. By combining a Pavlovian conditioning paradigm – in which the presentation of a rewarding sugar pellet was preceded by a light cue – and *in vivo* fiber photometry, the impact of short-term HE diet consumption on DA dynamics was investigated. Results revealed a significant decrease in cue-evoked DA in DR rats after HE diet exposure, contrasting with the unchanged response in DIO rats. This reduction in DA activity may signify reduced sucrose-reward salience in DR rats, potentially serving as an adaptive mechanism preventing excessive overeating and weight gain, consistent with their maintained body weight during exposure to high-energy diet. Moreover, DR rats exhibited lower motivation for the reward compared to DIO rats, indicating a differential response to the rewarding stimuli between the two groups. In conclusion, the study demonstrates how the mesolimbic DA system responds differently to HE diets in DIO and DR rats, shedding light on potential adaptive mechanisms that protect against excessive weight gain and altered motivation for rewards. Understanding these mechanisms could offer insights into managing obesity-related behaviors and associated neurobiological responses.

4:45 - 5:30 PM	Riverwalk A
Coffee Break & Exhibits	
5:30 - 7:10 PM	Ballroom III
Symposium 3: Alcohol Use Disorder Following Bariatric Surgery	

Chair(s): Allan Geliebter

5:30

Background And Potential Mechanisms Underlying Increased Alcohol Intake And Alcohol Use Disorder Following Bariatric Surgery

Allan Geliebter

Icahn School of Medicine at Mount Sinai, New York, NY, United States

Bariatric surgery is the most effective weight loss procedure for severe obesity. Sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB) are currently the most popular operations. Postsurgery, there is decreased desire for high energy-dense (HED) foods as well as increased risk for greater alcohol intake and alcohol use disorder (AUD). There may be a neurobiological basis for a transfer from HED intake to alcohol intake. In our lab using fMRI, we have shown that there is decreased reward activation in response to HED food cues following RYGB and SG. Also, we showed that reduced desire to eat following exposure to HED cues post RYGB correlated with reduced dorsal striatal activation to these cues. We also noted decreased scores on the Yale Food Addiction Scale concurrently with an increase in alcohol intake 2 y postsurgery. In this symposium, Allan Geliebter will present the background and potential mechanisms for increased alcohol intake postsurgery. Yanina Pepino will report her work on changes in alcohol absorption and in subjective effects of alcohol postsurgery as potential mechanisms. Andras Hajnal will provide suggestive evidence in rats that damage to the gastric branch of the vagus induced by gastric bypass surgery is a factor in increased alcohol intake. Lastly, Lisa Miller-Matero will discuss predictors of alcohol use disorder postsurgery and potential preventive and treatment approaches. Given the current volume of bariatric surgeries, it is essential to investigate the postsurgical increased alcohol-intake phenomenon, which may also help uncover new mechanisms for development of alcohol use disorder.

5:55

Impact Of Gastric Vagus Nerve On Alcohol Use And Stress: Relevance To Weight Loss Surgery

Andras Hajnal

Penn State Hershey College of Medicine, Department of Neural and Behavioral Sciences, and Department of Surgery, Hershey, PA, United States

The vagus nerve serves as a principal conduit for brain-body communication. Our studies in rat models undergoing gastric bypass surgery suggest that damage of the vagus nerve's gastric branch can lead to increased alcohol consumption. Therefore, we sought to examine the impact of gastric branch-selective vagotomy (VX) on alcohol intake and preference in multiple behavioral models, including continuous two-bottle choice, every-other-day two bottle access, drinking in the dark and conditioned place preference tests in the alcohol non-preferring Sprague-Dawley rat line. Our findings consistently demonstrated that VX led to an increase in alcohol consumption and preference in both male and female rats. Moreover, VX was found to elevate corticotropin-releasing factor (CRF) mRNA in the paraventricular nucleus of the hypothalamus (PVN) and was associated with increased levels of plasma corticosterone. Preliminary findings also reveal that chemogenetic activation of PVN oxytocin neurons reduces alcohol intake. These outcomes, together with electrophysiological evidence that VX reduces the ability of restraint stress to increase GABAergic signaling to putative PVN CRF neurons, suggest that the increase in CRF is due to a diminished regulatory effect of the vagus nerve on oxytocin signaling within the PVN, which normally helps control CRF activity. In fact, our research has also demonstrated that gastric branch-selective vagus nerve stimulation (VNS) elevates c-Fos expression in PVN oxytocin cells. Collectively, these promising findings call for the exploration of the vagus nerve, specifically through selective gastric VNS and its central signaling mechanisms, as innovative therapeutic strategies for treating alcohol use disorder.

6:20

Alcohol And Metabolic Surgery: From A Total Lightweight At The Bar To Binge Drinking.

M. Yanina Pepino

University of Illinois at Urbana-Champaign, Urbana, IL, United States

Metabolic surgeries, such as sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB), are highly effective in treating severe obesity, yet they are associated with an increased risk for alcohol use disorders (AUD). This presentation will focus on two mechanisms likely contributing to this risk. The first mechanism relates to the impact of RYGB/SG on alcohol pharmacokinetics. Both SG and RYGB accelerate alcohol absorption and heighten peak blood alcohol concentrations (BAC) in women. Despite differences in how these surgeries re-arrange the anatomy of the gastrointestinal (GI) tract, they both reduce the stomach size and thus similarly decrease the fraction of alcohol metabolized in the stomach before reaching the bloodstream. Therefore, both surgeries are associated with similar heightened peak BACs when women who have undergone metabolic surgery drink, compared to women who have had no surgery or have had laparoscopic gastric banding — a weight-loss surgery that leaves the GI tract unchanged. The second mechanism relates to changes in the subjective effects of alcohol and the development of alcohol tolerance. Previous research has shown that those who are less sensitive to the sedative effects of alcohol (i.e., can "hold their liquor") are at higher AUD risk. This presentation will discuss findings on how women with vs. without a history of metabolic surgery perceive the subjective effects of alcohol (given orally and IV using an alcohol clamp). Overall, the findings suggest that metabolic surgeries can lead to light-moderate drinking, resulting in BACs typically associated with binge drinking in individuals without surgery. This pattern of drinking is linked to increased health risk, the development of alcohol tolerance, and an elevated AUD risk.

6:45

Can We Prevent Alcohol Use Disorders After Metabolic And Bariatric Surgery?

Lisa R. Miller-Matero

Henry Ford Health, Detroit, MI, United States

Individuals who undergo bariatric surgery are at increased risk of developing an alcohol use disorder. The reasons for this increased risk are likely multifactorial and include changes in the pharmacokinetics of alcohol, increased sensitivity to alcohol, and coping with alcohol rather than food. Though the increased risk of an alcohol use disorder is well known, individuals continue to consume alcohol after bariatric surgery. As such, we need to identify ways to reduce risk. This presentation will discuss several hypotheses that we have examined to identify ways to prevent alcohol use disorders after bariatric surgery. These include exploration of whether patients understand their risk, if we can identify predictors of those who use alcohol after surgery, and whether patients may be underreporting their pre-surgical alcohol use. Research thus far has indicated that additional interventions are needed to prevent alcohol use disorders. Our team is developing and pilot testing a technology-based intervention to reduce alcohol use after bariatric surgery. Results from the open trial will be shared and directions for the next steps in this line of work will be discussed.

Oral Session 5: Hormones and Peptides

Chair(s): Wolfgang Langhans

5:30

Activation Of A Ghrelin-Responsive Neuronal & “Hunger” Ensemble In The Dorsomedial Hypothalamus Is Sufficient To Impact On Food Intake, Hunger Valence Evaluation And Food Motivation In Mice
 Iris Stoltenberg, Erik Schele, Renee Poelman, Suzanne L Dickson
 Gothenburg University, Gothenburg, Sweden

In the present study we sought to identify and functionally characterize an ensemble of candidate “hunger” neurones in the dorsomedial hypothalamus (DMH) that are activated by ghrelin in the fasting state. The ghrelin receptor is expressed in the DMH¹ and infusion of ghrelin into this brain area increases food intake², making the DMH an interesting candidate area. We utilised TRAP2 mice, in which activated (*fos*-expressing) cells co-express inducible Cre (CreER^{T2}) that enters the nucleus upon binding to 4-hydroxytamoxifen (4-OHT) leading to recombination, and in our case, expression of an activating designer receptor (hM3Dq) in TRAPed cells in the DMH. In this study, “hunger” neurones were TRAPed upon peripheral ghrelin injection in fasted mice, while fasted control mice received a saline injection. We found that chemogenetic activation increased food intake (1h; GhrelinTRAP 0.47±0.10 g vs SalineTRAP 0.04±0.02 g), food-motivated behaviour (assessed using a progressive ratio nose-poking for chow pellet paradigm; breakpoint GhrelinTRAP 340±106 nose pokes vs SalineTRAP 82±50 nose pokes) and also conditioned avoidance behaviour (in a conditioned place avoidance setup) in GhrelinTRAP (time spent in CNO paired chamber reduced from 621±29 sec to 479±37 sec) but not SalineTRAP mice (from 630±27 sec to 601±29 sec). These data show that activation of the ghrelin-responsive “hunger” ensemble in the DMH is sufficient to induce feeding-related behaviours. It highlights a role for these DMH “hunger” neurones in behaviours that extend beyond food intake to include food motivation and (hunger) avoidance.

¹ Zigman, J. M. *et al. J Comp Neurol* **494** (2006)

² Hyland, L. *et al. Physiol Behav* **220** (2020)

5:45

Chronic Glucagon Receptor-Agonism Requires Mediobasal Hypothalamic Gabaergic Signaling To Suppress Food Intake And Induce Tissue Thermogenesis.

Andrew J. Elmendorf^{1,2}, Betty Lorentz², Connor A. Mahler², Ellen Conceicao-Furber³, Ricardo J. Samms³, Jonathan N. Flak^{1,2}

¹Indiana University School of Medicine, Department of Pharmacology and Toxicology, Indianapolis, IN, United States,

²Indiana Biosciences Research Institute, Indianapolis, IN, United States, ³Eli Lilly and Company, Indianapolis, IN, United States

Glucagon receptor (GCGR)-mediated thermogenesis is a key component to the next-generation of obesity therapeutics. Our objective was to determine the physiologic mechanisms by which GCGR agonism induces sustained body weight loss. Chronic treatment of WT obese mice with a long-acting GCGR agonist (LAGCGRA) reduces body weight (BW), fat mass, and increases metabolic rate at thermoneutrality (28°C). Chronic LAGCGRA treatment progressively increases iBAT temperature (effect tripled by day 6), whereas $\beta 3$ agonism is less effective at stimulating thermogenesis over time (effect reduced by >50% by day 4). However, adipose tissue GCGR is not required for LAGCGR-mediated thermogenesis. So, there must be another mechanistic explanation. To determine if the LAGCGRA acts via central homeostatic circuits, we utilized *Vgat*^{fllox} (gene: *Slc32a1*) and *Vglut2*^{fllox} (gene: *Slc17a6*) transgenic mice. Upon mediobasal-hypothalamus (MBH) encompassing, adeno-associated virus mediated KO of glutamate signaling (*Vglut2*^{MBHKO}), we observed that LAGCGRA was just as effective at reducing BW by ~15% as GFP treated controls, but LAGCGRA only induced ~2% loss of BW in *Vgat*^{MBHKO} mice lacking GABA signaling. LAGCGRA also failed to increase iBAT temperature and reduce food intake, unlike the *Vglut2*^{MBHKO} mice. While hypothalamic glutamatergic cells may still release neuropeptides in response to LAGCGRA, these data show that MBH GABA signaling is required for the BW, adipose mass, tissue thermogenesis, and food intake effects induced by LAGCGRA. Future studies will define the hypothalamic population involved and locus of the LAGCGRA signal.

6:00

Amylin In The Amygdala Is Necessary And Sufficient For Feeding Behavior Control.

Suyeun Byun¹, Ivana Maric^{1,2}, Stina Borchers^{1,2}, Morgan R. Sotzen¹, Doris Olekanma¹, Mya A. Knappenberger¹, Matthew R. Hayes³, Karolina P. Skibicka^{1,2}

¹Department of Nutritional Sciences, Pennsylvania State University, State College, PA, United States, ²Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden, ³Department of Psychiatry, University of Pennsylvania, Philadelphia, PA, United States

Amylin, a pancreatic peptide, has a well-established role in feeding behavior control. Moreover, amylin analogues are already clinically utilized in patients with diabetes, and are under investigation as potential new anti-obesity pharmacotherapies. While area postrema has been recognized as a primary site for mediating amylin's satiating effects, more recent studies expanded this perspective to other brain regions, highlighting that our understanding of neural circuitry underlying actions of amylin on behavior remains incomplete. The central amygdala (CeA) recently emerged as a critical neural substrate for feeding behavior control and reward processing. We found that all components of amylin receptors (CTR, RAMP1-3) are expressed in the CeA; their potential role in physiology or behavior remains unknown. Therefore, here we investigated the

potential ingestive and motivated behavior roles of amylin in the CeA of male and female rats. We found that intra-CeA delivered amylin was sufficient to acutely reduce chow intake in both sexes, with this hypophagic effect lasting longer in females. Intra-CeA amylin also potentially reduced food-motivated behavior for sucrose. However, when high-fat and sucrose were offered, intra-CeA amylin selectively reduced the high-fat food intake, while sparing the sucrose intake. Pharmacological blockade of CeA amylin receptors increased food intake, but only in female rats. Virogenetic knockdown of CTR resulted in increased body weight gain in females, but not males. Our data indicate the CeA as a novel neural substrate for amylin. They reveal amylin receptors in the CeA are sufficient to alter feeding behavior in both sexes, while necessary only in females, underscoring a sex difference in the necessity of the CeA amylin signaling.

6:15

Beta-Glucan Supplementation Reduces Food Intake And Body Weight Gain In Hf-Fed Rats By Altering Meal Patterns And Improving Cck Sensitivity.

Lindsey K. Macias^{1,2}, Jasmine Shakir¹, S. Andrew Aston^{1,2}, Jackson H. Freiman¹, Brianna C. Bullock¹, Akul Kesarwani¹, Timothy H. Moran¹, Kellie L. Tamashiro^{1,2}

¹Psychiatry and Behavioral Sciences, Johns Hopkins School of Medicine, Baltimore, MD, United States, ²Cellular and Molecular Medicine Graduate Program, Johns Hopkins School of Medicine, Baltimore, MD, United States

Previous studies show that high-fat (HF) diets promote obesity by inducing hyperphagia and altered meal patterns. β -glucan (BG), a soluble dietary fiber, is shown to increase satiety by delaying gastric emptying and small intestinal transit due to its viscoelastic properties. We hypothesized that BG supplementation would prevent HF-induced obesity and hyperphagia by altering meal patterns and preserving cholecystokinin (CCK)-induced satiety. To address this question, 24 male Sprague Dawley rats (~250 g) were randomly assigned to 3 diet groups (n=8): chow diet (CH; Envigo 2018, 18% kcal fat), high-fat diet (HF; Research Diets D12492, 60% kcal fat), or custom high fat- β -glucan diet (HFBG; Research Diets, 60% kcal fat, 10% oat β -glucan). HF rats were hyperphagic compared to CH rats while HFBG rats had similar food intake to CH. By day 18, both HFBG (394 ± 3 g) and CH rats (399 ± 4 g) had lower body weight compared to HF (419 ± 3 g). Using the BIODAQ system, meal pattern analyses showed that meal size was greater in HF rats (12.9 ± 1.1 kcal) compared to CH (10.1 ± 0.4 kcal), while HFBG meal size (12.3 ± 0.4 kcal) was in between HF and CH. HFBG rats ate fewer meals (6.1 ± 0.2) compared to the CH group (7.8 ± 0.5) and HF group (7.5 ± 0.5). Reduced meal frequency in HFBG rats suggests that BG increases satiety. To test responsiveness to the satiety hormone CCK, rats were fasted for 6 h and injected with either saline or CCK (3 or 6 μ g/kg, IP) immediately prior to food access. CH and HFBG animals suppressed food intake 30 min after injection in response to both doses of CCK compared to saline. The HF group did not respond to either dose of CCK. We conclude that β -glucan supplementation prevents weight gain on HF diet by altering meal patterns and preserving CCK sensitivity.

6:30

Contributions Of Prolactin-Releasing Peptide (PrRP) In Catecholaminergic Neurons To Fasting-Induced Feeding, Sweet Tastant Preference, And Affective Behaviors

Caitlyn M Edwards^{1,2}, Danny G Winder¹, Richard B Simerly²

¹University of Massachusetts Chan Medical School, Worcester, MA, United States, ²Vanderbilt University, Nashville, TN, United States

Prolactin-releasing peptide (PrRP) is a neuropeptide predominantly expressed in neurons within the dorsomedial hypothalamus (DMH), nucleus of the solitary tract (NTS), and ventrolateral medulla (VLM). In the NTS and VLM, PrRP expression substantially overlaps with the A2/A1 noradrenergic populations, which are known to influence food intake and anxiety-related behaviors. Despite the responsiveness of PrRP+ neurons to changes in energy balance, the specific role of PrRP in these neurons remains largely unexplored. In this study, we utilized a genetic approach by crossing tyrosine hydroxylase (TH)-Cre and PrRP-Flox mouse lines to achieve PrRP knockdown in A2 and A1 noradrenergic neurons. Our investigation aimed to elucidate the involvement of PrRP expression in these neurons in feeding behavior following a fast, saccharin preference, and various affective behaviors. Our findings reveal that PrRP knockdown in TH+ neurons leads to a significant increase in food intake after an overnight fast, along with heightened preference for saccharin, particularly evident in female mice. Furthermore, we observed a marked increase in immobility time in the forced swim test, while no significant effects were noted in the open field, elevated plus maze, or light/dark box tests. Additionally, we explored the impact of PrRP expression in these neurons on neuronal responses to the gut peptide, cholecystokinin (CCK), by examining cFos following an intraperitoneal injection of 5mg/kg CCK. Our results collectively implicate A2/A1 PrRP expression in regulating homeostatic feeding, hedonic non-caloric tastant intake, and behavioral responses to stress. These findings will be discussed within the broader context of PrRP's involvement in modulating neuronal responses to vagal stimulation.

Characterizing Sex Differences In Brainstem Glp-1 Control Of Sensory-Specific Satiety

Sarah V. Applebey, Allison G. Xiao, Benjamin C Reiner, Matthew R Hayes
University of Pennsylvania Philadelphia, Philadelphia, PA, United States

Meal variety promotes overconsumption by delaying sensory-specific satiety (SSS), the transient reduction in reward value of a recently consumed food. While SSS suppresses intake of eaten foods, it increases the relative value of different, uneaten foods. Thus, a varied meal can delay meal termination and promote caloric overconsumption. Despite its role in meal cessation, the neuroendocrine mechanisms underlying SSS are largely unknown. Here, we developed a model of SSS to investigate the brainstem action of one satiation signal, glucagon-like peptide-1 (GLP-1), in SSS. Compared to the same food presented a second time, male rats consumed more of a different food. Using 4th ICV delivery of a GLP-1R agonist or antagonist, we demonstrated GLP-1 receptors (GLP-1Rs) in the brainstem are critical for the SSS-induced decline in same food intake and are sufficient to prevent overconsumption of a different food. Together, these data suggest brainstem GLP-1 signaling is attenuated in the presence of a different (but not the same) food to enable overconsumption. In our SSS model, female rats overconsumed the different food in all but one phase of the estrous cycle, estrus. However, 4th ICV injection of GLP-1R agonist exendin-9 selectively restored overconsumption of the different food during estrus. qPCR analysis revealed greater expression of GLP-1R and GLP-1 precursor, preproglucagon, in the caudal brainstem of female rats sacrificed during estrus. These data indicate endogenous increases in brainstem GLP-1 action during estrus are sufficient to prevent different food overconsumption. Combined with our pharmacological investigations in males, our experiments identify a role for brainstem GLP-1 control of sensory-specific satiety. NIH-DK13744

State-Dependent Activity In Hindbrain Glp-1-Producing Neurons Regulates Consummatory And Valence Behavior Through Interconnected Hypothalamic And Limbic Circuits

Miguel Duran¹, Sonja Virkus¹, Christian Lopez¹, Kylie McMichen¹, Yaslle Andrade Cavalcante Moraes¹, Eshita Yadav¹, Joti Singh¹, Zoe Fokakis¹, Samantha Stocking¹, Samuel Poole², Chad Hunter², Kirk Habegger², J. Andrew Hardaway¹
¹Department of Psychiatry and Behavioral Neurobiology, University of Alabama at Birmingham, Birmingham, AL, United States, ²Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, United States

Glucagon-like peptide 1 (GLP-1) therapeutics have experienced a meteoric rise in adoption, but our understanding of the endogenous systems that produce GLP-1 and how they regulate behavior remain incomplete. Preproglucagon neurons in the nucleus of the solitary tract (*Gcg*^{NTS} neurons) are the primary source of GLP-1 in the brain. In this study, we examined the neurophysiological and causal contributions of *Gcg*^{NTS} neurons to consummatory and valence behavior. Using electrophysiology, we observed that *Gcg*^{NTS} neuron neural firing and excitability is reduced in response to 24-hour food deprivation that varied by sex. Conversely, *Gcg*^{NTS} neurons significantly increase their firing rate after a brief 1-hour chow refeed after food deprivation. Consistent with this finding, *Gcg*^{NTS} neurons display elevated Fos levels following binge-like consumption of palatable high-fat diet. Using *in vivo* optogenetics, we observed that optogenetic activation of *Gcg*^{NTS} neurons produced both anxiety and negative valence that varied by sex. High-frequency activation of *Gcg*^{NTS} neurons also reduced feeding and appetitive behavior. Interestingly, high-frequency activation of *Gcg*^{NTS} neurons produced lasting effects that persisted after the cessation of laser illumination. Using a novel transgenic mouse, *Gcg*-*IRES*-FlpO, crossed to *Glp1r*-Cre mice combined with viral and transgenic reporters, we found that *Gcg*^{NTS} neurons and *Glp1r* neurons in the hypothalamus and amygdala make reciprocal connections. Currently, we are using optical tools to measure functional connections between *Gcg*^{NTS} neurons and *Glp1r* neurons in the paraventricular nucleus of the hypothalamus and amygdala.

Friday, July 12, 2024

8:00 - 5:15 PM	Sheraton Promenade West
Registration	
8:30 - 10:15 AM	Riverwalk A
Poster Session 3 & Exhibits	

P300 **High-Fat Fiet-Induced Hyperphagia And Body Weight Gain Depend On Sex And Fatty Acid Chain Length.**

Brent B. Bachman, Kimberly P. Kinzig
Purdue University, West Lafayette, IN, United States

To study diet-induced energy intake and body weight gain in preclinical rodent models, one popular method is to provide ad libitum access to a high-fat diet (HFD). However, previous studies have demonstrated that a HFD is less effective in female rats than in male rats; and its effects are attenuated by a dietary shift from long-chain triglycerides (LCT) to medium-chain triglycerides (MCT). However, it is still unknown how these two factors may interact. Here, we aimed to compare the effects of four different 63% HFDs (two rich in LCT and two rich in MCT) on energy intake and body weight gain in adult male and female rats over two experiments. In experiment 1, we compared a HFD diet rich in vegetable shortening (HFD-LCT) to a HFD diet rich in C8/C10 triglycerides (HFD-MCT); and in experiment 2, we compared a HFD rich in red palm oil (PALM) to a HFD rich in coconut oil (COCO). In both experiments, our main hypothesis was that there would be a three-way interaction between diet type, sex, and time, such that the HFD rich in MCT would attenuate energy intake and body weight gain over time compared to the HFD rich in LCT, but that females would be less affected by either type of HFD than males. In experiment 1, contrary to our hypothesis, there was not a significant three-way interaction. However, consistent with earlier reports, across sex, there was a significant two-way interaction between diet and time, such that HFD-LCT gained more weight than HFD-MCT. In experiment 2, however, consistent with our hypothesis, there was a significant three-way interaction, such that PALM gained more weight than COCO only in females. As these results indicate, HFD-induced energy intake and weight gain in rats depends on the interaction between sex and fatty acid composition.

P301 **Reinforcing Value Of Hyperpalatable And Non-Hyperpalatable Foods In Adolescents**

Katelyn A Carr¹, Jennifer L Temple²

¹Pediatrics, University at Buffalo Jacobs School of Medicine, Buffalo, NY, United States, ²Exercise and Nutrition Sciences, University at Buffalo School of Public Health and Health Professions, Buffalo, NY, United States

Hyperpalatability is a categorization for foods focusing on how combination of nutrients, including carbohydrates, fat, sugar, and salt, impact food wanting and energy intake. Hyperpalatable foods (HPFs) have been categorized as fat-sugar (donuts), fat-sodium (potato chips) and carb-sodium (pretzels). Current research has shown that HPFs are related to greater energy intake and greater likelihood to gain weight over 1-year, but no research has examined reinforcing value of food (RV_{FOOD}), or motivation, for HPFs. Comparison of RV_{FOOD} between HPFs and non-HPFs as well as between fat-sugar (1 food) and fat-sodium (3 foods) and double-category fat-sugar/fat-sodium HPFs (2 foods) was examined in a sample of 215 adolescents 12-14 years old. Adolescents completed a reinforcing value task of a chosen HPF and a chosen non-HPF in separate sessions. This task consisted of a progressive ratio schedule for snack food and a non-food alternative. RV_{FOOD} was scored using the area-under-the-curve for total responding and log-transformed. ANOVA was used to examine main effects of HPF category, differences between HPF and non-HPFs and their interaction on RV_{FOOD}. There was a significant main effect of HPF vs. non-HPF ($F(1,212)=22.2, p<0.001$), with HPFs having higher RV_{FOOD}. There was a significant main effect of HPF category ($F(2,212)=6.4, p=0.002$, with fat-sugar foods having higher RV_{FOOD} than fat-sodium and double-category foods. There was also an interaction between HPF category and HPF vs. non-HPF ($F(2,212)=4.9, p=0.008$), with double HPF foods having a greater difference in RV_{FOOD} to non-HPFs than fat-sugar or fat-sodium alone. This shows RV_{FOOD} differences between HP foods and non-HP foods, suggesting that these macronutrient combinations are related to greater motivation to eat.

P302 **The Role Of Vasopressin Deficiency In The Fluid Intake Suppression Hypersensitivity To Central Glucagon-Like Peptide-1 In The Brattleboro Rat**

Sydney A David¹, Destiny J Brakey², Matthew J Paul¹, Derek Daniels^{1,2,3}

¹Department of Psychology, Buffalo, NY, United States, ²Department of Biological Sciences, Buffalo, NY, United States,

³The Center for Ingestive Behavior Research, Buffalo, NY, United States

Physiologically and behaviorally, fluid and food intakes are entangled. There is overlap in the brain regions that control the two ingestive behaviors, and signaling peptides that affect one often affect the other. For example, glucagon-like peptide-1 (GLP-1) suppresses both food intake and fluid intake. The vasopressin-deficient Brattleboro rat has emerged as a potential model organism to separate fluid intake from food intake and could help isolate brain regions, particularly involved in fluid intake control. Brattleboro rats drink copious amounts of water, but eat a similar amount of food when compared to wildtype rats. Also, Brattleboro rats are hypersensitive to the fluid intake suppression caused by central administration of a GLP-1

receptor agonist, extendin-4 (Ex4), with no differences in sensitivity to the food intake effects. To evaluate if the hypersensitivity is directly related to the untreated vasopressin deficiency in these rats, we implanted osmotic mini pumps containing desmopressin (ddAVP, a vasopressin type 2 receptor agonist) and tested for fluid intake suppression by Ex4. We found that ddAVP reduced, but did not completely prevent, the hypersensitivity to Ex4, suggesting both correctable and uncorrectable changes underlying the response to Ex4. Ongoing experiments are testing if treatment with tolvaptan in wildtype rats (a vasopressin type 2 receptor antagonist) produces the hypersensitivity to Ex4 observed in Brattleboro rats. Together with previous work, these data provide useful context that will help identify the underlying cause of the different responses.

P303

Neural Underpinnings Of Food Fussiness In Adolescence

Sarah Ann Duck, Elena Jansen, Liuyi Chen, Susan Carnell
Johns Hopkins University School of Medicine, Baltimore, MD, United States

Food fussiness may increase risk for malnutrition and eating disorders, meriting investigation of its biological underpinnings. Adolescents (14-18y, n=86) completed an fMRI task during which they viewed photos of fruits and vegetables [F&V], palatable energy-dense foods, and non-foods, in fasted (474 ml water, 0 kcal) and fed (474 ml of milkshake, 480 kcal) conditions on separate days. Following scanning on each day, they completed a multi-item ad libitum meal. Parents completed the Child Eating Behavior Questionnaire [CEBQ]. Adolescents reported habitual dietary intake over one day using ASA24. Adolescents were categorized based on CEBQ Food Fussiness [FF] scores (range 1-5), such that scores >3=high FF (n=23), and scores <2=low FF (n=28), and compared using t-tests with $p<.05$ considered significant. Bayesian inference implemented in SPM12 with an effect size threshold of Cohen's $d=0.2$ and a Bayes factor threshold of $\log BF=3$ was used to generate brain activation maps. Groups did not differ on age or BMIz. The high vs. low FF group reported lower wanting for F&V in the fMRI task and consumed lower absolute and relative intake of fruits and vegetables at the ALM, in both the fasted and fed conditions, while ASA24 data demonstrated greater % calorie intake from added sugar. Group differences in brain activation were most apparent for the F&V vs. non-food contrast in the fed condition, such that the high vs. low FF group showed greater activation to F&V in widespread regions implicated in object processing, decision-making and interoception (middle temporal and occipital gyri, precuneus, inferior parietal lobule, superior frontal gyrus, insula). Further understanding of the neural basis of food fussiness could aid development of biobehaviorally-informed interventions.

P304

The Relationship Between Adolescent Nutrition Beliefs And Food Insecurity

Kristiana/M Feeser, Jennifer/L Temple
University at Buffalo, Buffalo, NY, United States

Introduction: Beliefs about “healthy” eating contribute to eating behavior and overall health. During adolescence, these beliefs intersect with growing autonomy over eating choices and may be influenced by other factors, such as food and nutrition insecurity. The primary goal of the current study was to use a qualitative methods approach to understand how adolescents’ beliefs and attitudes about nutrition are related to food and nutrition insecurity. **Methods:** Utilizing a semi-structured interview and thematic analyses, nutrition beliefs and knowledge from 30 adolescents (11-14 years old) from low-to moderate-income households were examined. This interview was part of a larger, longitudinal study called UB-EATS (University at Buffalo Eating Among Teens Study) in which teens visited the lab six times over a two year period. At the end of the third visit, participants were interviewed using an interview guide adapted from the original by Beck and colleagues. In this interview, participants were asked a series of questions about healthy eating, the effect of mood on food choice, eating habits, cooking, and food shopping. **Results:** While nutrition beliefs (e.g., name a health and unhealthy food; do you have a healthy diet) did not differ between food secure and insecure participants, perceived presence of healthy foods within the home did (e.g., what healthy foods are in your home right now). **Conclusion:** Adolescents with food insecurity perceived less healthy foods available in the home (i.e. listing fewer healthy foods choices at home currently). Adolescents did not differ in beliefs about nutrition (i.e. what foods are healthy and not healthy; current diet healthiness) based on nutrition security status.

P305

Investigating The Effects Of Altering Portion Size Reduction Awareness On Compensatory Eating Behaviour.

Thomas FM Gough¹, Jane Brealey¹, Amy Finlay¹, Andrew Jones², Eric Robinson¹

¹University of Liverpool, Liverpool, United Kingdom, ²Liverpool John Moores University, Liverpool, United Kingdom

Portion size of food is a reliable determinant of food intake. Reducing portion sizes of foods may be an effective public health intervention, however later compensatory food intake may partially negate an overall reduction in food intake. The present study investigates how reducing portion size of a lunch meal can affect later food intake, focussing on both physiological and psychological factors. 108 participants will attend two lab sessions for lunch and dinner, where participants are given ad libitum access to each meal. In the second session, the portion size of the lunch meal will be manipulated, producing three conditions: participants will be served the amount of pasta consumed in the previous session and will be told this (control condition); participants will be served 15% less than the amount of pasta consumed in the previous session and will be told this (reduced aware condition); participants will be served 15% less than the amount of pasta consumed in the previous session, but will be told that the portion size was the amount as what they consumed in the previous session (reduced unaware condition). We expect to find that immediate post-lunch intake will be greater in both reduction conditions, driven by physiological processes, however we expect to find that later post-lunch intake will be greater in the reduced aware condition compared to the other two conditions, due to psychological processes (i.e., episodic memory of how much food participants were told they were served), affecting later post-lunch intake. These findings will provide an understanding of the causes of compensatory eating behaviour in relation to reduction of portion size. Data collection will be completed in May 2024 and results will be presented at the conference.

P306

Sipping Pressure Via Sipometer As A Measure Of Motivation Predicts The Size Of A Meal Eaten To Capacity Before, And Weight Loss After, Bariatric Surgery

Jeon D. Hamm^{1,2}, Blandine Laferrere³, Jeanine Albu⁴, Subhash Kini⁵, Harry R. Kissileff²

¹Howard University College of Medicine, Washington, DC, United States, ²Diabetes, Obesity, & Metabolism Institute, Icahn School of Medicine at Mount Sinai, New York, NY, United States, ³Division of Endocrinology, Columbia University

Irving Medical Center, New York, NY, United States, ⁴Division of Endocrinology, Department of Medicine, Mount Sinai Morningside Hospital, New York, NY, United States, ⁵Institute of Bariatric and Minimally Invasive Surgery, Mount Sinai Morningside Hospital, New York, NY, United States

We previously reported (SSIB 2022) that the size of laboratory meals eaten to capacity (CapMeal) before bariatric surgery predicted percent weight loss (%WL) after surgery ($p < .05$). We currently test whether the motivation to consume sweet liquids also predicts %WL and if CapMeal is a mediator of this relationship. Before, and 2-y after, bariatric surgery, patients completed two tasks. Task 1: Patients were tested for motivation to consume sweet liquids by sipping and spitting a sweet low-cal beverage under ad lib (AL) and progressive ratio reinforcement (PR, increments of 3 sec) schedules. Task 2: Patients consumed a liquid meal of chocolate Ensure® to capacity. Cumulative pressure (CumPres), a measure of effort, hence motivation, was the sum of the pressures exerted during Task 1 between reinforcements. Body weight was recorded before and after surgery. Linear regressions (proc GLM) of %WL and CapMeal from CumPres, under AL and PR conditions, and mediation analyses (%process), were run. CumPres under PR predicted CapMeal ($b = 0.95 \text{ PSI/g} \pm 0.392 \text{ SE}$, $R^2 = 0.136$, $p = 0.02$), and %WL at 1-y ($b = -0.035\%/\text{PSI} \pm 0.012 \text{ SE}$, $R^2 = 0.211$, $p = 0.0048$) and 2-y ($b = -0.0425 \text{ PSI}/\% \pm 0.0167 \text{ SE}$, $R^2 = 0.151$, $p = 0.015$). In the mediation models, the indirect effect of CumPres under PR on the prediction of %WL through CapMeal (normal theory test for indirect effect) was small ($b = -0.009 \text{ g}/\% \pm 0.006 \text{ SE}$) and not significant ($p = 0.16$) at 1-y and $-0.015 \text{ g}/\% \pm 0.009 \text{ SE}$ ($p = 0.104$) at 2-y. CumPres under AL did not predict CapMeal or WL ($p > 0.05$). In conclusion, meal size was not a mediator between baseline motivation to consume sweet liquids and weight loss. Therefore, while motivation influences intake capacity, these two variables are independent predictors of post-surgical weight loss.

P307 **Greater Threat Perception During A Mental Stressor Enhances The Association Between Post-Stress Anxiety And M&M Intake**

Rebecca Klatzkin¹, Alexandra Babij¹, Laurence Nolan²

¹Rhodes College, Memphis, TN, United States, ²Wagner College, Staten Island, NY, United States

Stressors are associated with a shift in preference towards comfort foods, yet there is wide variability in the amount of food consumed under stress. Variability in stress-eating may be explained in part by individual differences in perceptions of threat or challenge during the stressor. Greater perceptions of threat occur when the demands of a stressor outweigh the resources or the ability to cope and are associated with negative psychophysiological responses and lower performance outcomes. No study to date has examined how our perceptions of threat during a stressor impacts stress-eating. We predicted greater perceptions of threat during a mental stress task would strengthen the association between stress-induced anxiety and snack intake. 39 undergraduate women underwent a laboratory-based mental stress task before rating their perceptions of threat during the stress task and tasting four snacks: M&Ms, chips, veggie straws, and raisins. The moderation model (PROCESS model 1) was significant, $F(5,33) = 3.41$, $p = 0.014$; $R^2 = 0.34$. Greater stress-induced anxiety was associated with eating more M&Ms only for women with greater threat perception during the stressor ($b = 0.03$, $SE = 0.012$, $p = 0.009$; 95%CI: $0.01 - 0.06$). Thus, greater perceptions of threat during a stressor may enhance stress-induced anxiety as a trigger for unhealthy comfort food intake. Replications in larger samples may inform obesity-related clinical treatments that target state perceptions of stress.

P308 **Relations Of Eating In The Absence Of Hunger During Pregnancy With Weight Outcomes, Eating Behaviors, Sleep Quality, Stress, And Depressive Symptoms.**

Leah Lipsky¹, Kyle Burger², Grace Shearrer³, Tonja Nansel¹

¹Social and Behavioral Sciences Branch, Division of Population Health, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD, United States, ²University of North Carolina - Chapel Hill, Gillings , Chapel Hill, NC, United States, ³University of Wyoming, Laramie, WY, United States

Objective: Eating in the absence of hunger (EAH) may lead to weight gain. This study examined correlates of EAH in pregnancy and postpartum. **Methods:** Early pregnancy BMI, gestational weight gain, postpartum weight loss, and returning to early pregnancy weight were calculated from anthropometrics measured from <12 weeks gestation to 1 year postpartum. Participants reported baseline eating behaviors (Dutch Eating Behavior Questionnaire), depressive symptoms (Edinburgh Postnatal Depression Scale), stress (Perceived Stress Scale), and sleep quality (Pittsburgh Sleep Quality Index). In the 2nd trimester, $n = 46$ participants completed two EAH assessments, one of minimally-processed (raw fruit, unsalted roasted peanuts, raw vegetables) and one of highly-processed foods (cookies, brownies, candy, chips, cheese popcorn). EAH (kcal) all foods, and of sweet (fruit/desserts) and savory (vegetables/salty snacks) foods separately, were calculated for each assessment (6 variables). Relations were estimated using linear and multinomial logit regression models. **Results:** Emotional eating was positively related to EAH of highly processed savory foods ($\beta \pm SE = 42.3 \pm 20.9 \text{ kcal}$, $p = 0.049$), while sleep quality was inversely related to EAH of minimally processed savory foods ($7.0 \pm 2.6 \text{ kcal}$, $p = 0.009$). Depressive symptoms, stress, restrained eating, and external eating were not associated with any EAH measure. EAH was not associated with weight outcomes, except that EAH of minimally processed foods ($OR = 0.99$, 95%CI = $0.98 - 1.00$, $p = 0.06$) was modestly associated with lower odds of returning to early pregnancy weight by 12 months postpartum. **Conclusion:** EAH in pregnancy was not consistently or robustly related to eating behaviors, depressive symptoms, sleep quality, stress, or pregnancy-related weight change.

P309 **Divergent Changes In Social Stress-Induced Motivation In Male And Female Mice**

Megan McGraw, Cooper Christensen, Hailey Nelson, Ai-Jun Li, Emily Qualls-Creekmore
Washington State University, Pullman, WA, United States

Stress has been shown to dysregulate motivated behaviors in a bidirectional manner depending on the nature of the stressor. Social defeat stress is a common model used to study stress-induced motivation changes, however, historically this model excluded females due to the lack of female-to-female aggression and unreliable male-to-female aggression in rodents. Additionally, changes in motivation are often assessed well after stress exposure ends, potentially occluding changes to motivation that occur during stress. Recently, the chronic non-discriminatory social defeat stress (CNSDS) model demonstrated social defeat of male and female C57BL/6J mice by exposing both mice to an aggressive male CD1 mouse

simultaneously. Using this model, we compared changes in the motivated behavior of male and female mice throughout chronic stress, rather than only after. We hypothesized that stress-induced changes in motivated behavior would be most pronounced during the stress exposure period. To test motivated behavior, we used the Feeding Experimental Device (FED3.1), a home cage device for operant responding. Motivated behavior was tested prior to, during, and after CNSDS by measuring nose pokes for sucrose pellets on a progressive ratio schedule of reinforcement. Our results demonstrated divergent outcomes of motivated behavior where male mice increased operant responding only during CNSDS, but female mice exhibited a decrease in operant responding throughout and after CNSDS. This study highlights the need to investigate the effects of stressed-induced motivation over time, as well as the increased need to understand differences in the stress response in females.

P310 **Flavor-Nutrient Learning Is Either Positively Associated, Negatively Associated, Or Not Associated With Individual Differences In Obesity Proneness In Rats.**

Kevin P. Myers
Bucknell University, Lewisburg, PA, United States

In rodent models, learned associations between a food's taste/flavor and the rewarding effects of nutrients sensed in the gut or post-abortively typically increase preference, meal size, and total intake. Flavor-nutrient learning is thus often presumed to be obesogenic by promoting choice and intake of energy-dense foods. However, evidence linking flavor-nutrient learning and weight gain is ambiguous and limited published data comparing lean and obese rats shows conflicting results. This presentation reports experiments designed to determine whether rats who are more obesity-prone are also more (or less) responsive to flavor-nutrient learning, and if so, whether differences in flavor-nutrient learning precede or follow obesity. Contrary to our previously published demonstration that rats gaining the most weight on a high-fat/sugar diet subsequently show stronger flavor-nutrient learning, in a study of young, lean rats, those showing the strongest behavioral response in a flavor-nutrient learning protocol were subsequently more resistant to weight gain on a cafeteria diet. Further studies comparing two rat strains (DIO vs DR) selectively bred to be prone or resistant to diet-induced obesity found no apparent differences in several measures of flavor-nutrient learning. Thus, across several studies, individual differences in obesity proneness were either positively correlated, negatively correlated, or uncorrelated with proneness to diet-induced obesity, calling for a more nuanced view of how gut appetite signals influence intake and energy balance. Results from these experiments collectively show that the relationship between flavor-nutrient learning and weight gain is not straightforward and may change dynamically with the onset of obesity.

P311 **Disordered Eating Behavior, Sensitization, And Food Security Status: A Cross-Sectional Analysis In Low-Income Adolescents.**

Ana Leticia Pereira Andrade^{1,2}, Jennifer L Temple^{1,2,3}

¹. Department of Community Health and Health Behavior, University at Buffalo, Buffalo, NY, United States, ²Center for Ingestive Behavior Research, University at Buffalo, Buffalo, NY, United States, ³Department of Exercise and Nutrition Sciences, University at Buffalo, Buffalo, NY, United States

Introduction: Disordered eating behaviors (DEBs), such as binge eating and restrictive eating, often present a risk for the mental and physical health of individuals. The relationship among DEBs, food insecurity (FI) status and sensitization of the relative reinforcing value (SENS) is complex and multifaceted. Further, there are often differences between parent-reported household FI status and child reported FI status in relation to DEBs. This study aimed to investigate associations between DEBs and FI status, both parent and adolescent-reported, and to explore the mediating role of SENS in these relationships. **Methods:** 99 low-income adolescents (11-14 years old) participated in the University at Buffalo Eating Among Teens, 2-year prospective cohort study. Participants completed the Eating Disorders Examination Questionnaire (EDE-Q) and performed behavioral tasks to assess RRV of food and SENS. FI status was analyzed through adolescent and parents/guardians survey responses. Hierarchical linear regression models were used to analyze these relationships, with adjustments for biological sex and child age. **Results:** At baseline, we found no relationships between EDE-Q scores and parent reported FI status (all $p > 0.1$). However, we found that those with higher adolescent-reported FI scores had significant higher scores on the EDE-Q Global ($p = 0.038$) and the EDE-Q Shape and Weight Concerns ($p = 0.009$) subscale. **Conclusion:** Adolescents with perceived FI experienced heightened DEBs; but this relationship was not mediated by higher SENS to palatable foods. These results might be related to factors such as stigma, awareness, parental comprehension, control over food, and peer influence. This highlights the importance of assessing adolescent perceptions of FI in identifying DEBs

P312 **Exploring The Impact Of Diet And Ultra-Processed Foods On Working Memory In Children And Parents**

Ingrid Rivera-Iniguez, David R. Strong, Kyung Rhee, Dawn M. Eichen, Kerri N. Boutelle
University of California San Diego, San Diego, CA, United States

Ultra-processed foods (UPFs) are made by industrial processes that increase their content of energy density, fats, sugars, and sodium, to make them hyper-palatable. Diets rich in UPFs are related to obesity and impact brain functioning. Given the role executive function (EF) has in food decision-making, we wanted to evaluate the relationship between diet and UPFs with EF among children and their parents presenting for a weight-management trial. 141 parent-child dyads (child age=9.9y(1.3), BMI_z=2.0 (0.3), 67% female, 31% Hispanic, 44% White, 25% Other; parent age=43y(6.6), BMI=32(6.4), 82% female)

completed anthropometrics, EF measures (the Digit Span Backward (DSB), the Stop Signal Task (SST) and the Wisconsin Card Sorting Test (WCST)) and three 24-hour dietary recalls before treatment. Foods from the 24-hour dietary recalls were classified as UPFs using the NOVA classification system and presented as servings and as percentages from total energy. Linear regression models controlling for age, gender, race, and BMI/BMIz evaluated the relationship between EF and UPFs/nutrients. Energy consumption from UPFs was 54% for parents and 61% for children. Among parents, lower DSB was correlated with overall UPFs servings ($\rho=-.24, p<0.001$), total energy ($p=0.03$); carbohydrates kcal ($p=0.04$), saturated fats grams ($p=0.008$), sodium grams ($p<0.001$), servings from UP vegetables ($p=0.03$). In children, lower DSB was associated with the percentage from UP Meats ($p=0.009$). No relationships were found with SST or WCST. These results show that lower working memory is associated with higher consumption of calories, carbohydrates, saturated fats, and sodium in parents and UP meats in children. Future research could focus on targeting the reduction of UPFs and other deleterious nutrients.

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What And When People Eat; 2 Weeks Of Self-Reported Data From 10,000+ Participants

Tyler Tran, Jialu Tsui, Joey Hou, Emily Manoogian, Satchidananda Panda
Salk Institute for Biological Studies, La Jolla, CA, United States

What and when people consume food, supplements, and medicines are important determinants of health. These parameters often vary from day to day, yet there is very little information on what and when people consume for at least a week. Using the myCircadianClock smartphone app, we collected self-reported intake of food, beverage, medication and supplements. After informed consent, participants were encouraged to self-report their ingestive behavior for at least two weeks. They were prompted to log these items using their own natural language and were not required to specify portion size or quantity of items consumed. Their intake log and accompanying time-stamps were encrypted and transmitted to a server. A custom annotation pipeline and food nomenclature was used to identify items consumed. Participants who reported at least two caloric food or beverages 5 h apart within a 24 h day (between 4am and 3:59am) for at least 10 out of 14 days were considered compliant and their data were used in further analyses. To describe day to day variation in food timing, we used three different parameters: average time of first and last energy intake, mid 95%tile interval of energy intake and the median time of all energy intake. To describe the variety of food consumed, we calculated the number of unique foods or beverages consumed. From >5 million analyzed logs of items consumed, >90% were matched to a known food, beverage, medication, or supplement. Over 10,000 people were considered compliant for >10 out of 14 consecutive days, with more than 50% of these participants logging at least one supplement or medication. Participants showed large variations in various parameters describing the timing of food intake and the diversity of foods and beverages consumed.

P314

Effect Of Ultra-Processed Foods On Delay Discounting Rate AMong YOUNG ADULTS

Wenjing Yu^{1,2}, Emma H. Leslie^{1,3}, Maria Rego⁴, Monica Ahrens⁵, Alexandra L. Hanlon⁵, Valisa E. Hedrick⁴, Kevin P. Davy⁴, Benjamin Katz⁶, Brenda Davy⁴, Alexandra G. DiFeliceantonio^{2,3}

¹Fralin Biomedical Research Institute, Virginia Tech, Roanoke, VA, United States, ²Department of Biology, Virginia Tech, Blacksburg, VA, United States, ³Graduate Program in Translational Biology, Medicine, and Health, Virginia Tech, Blacksburg, VA, United States, ⁴Department of Human Nutrition, Foods, and Exercise, Virginia Tech, Blacksburg, VA, United States, ⁵Center for Biostatistics and Health Data Science, Virginia Tech, Roanoke, VA, United States, ⁶Department of Human Development and Family Science, Virginia Tech, Blacksburg, VA, United States

Ultra-Processed Food (UPF) are widely consumed in the US and it is argued that UPFs lead to obesity and poor health outcomes. Meanwhile, Delay Discounting (DD) is a well-validated measure of impulsivity that measures individuals' valuation of future monetary reward versus a smaller, immediate reward. Higher DD is proposed to be associated with impulsive behavior and negative health outcomes. The objective is to measure the association of DD and dietary intake. Here, we used data from an ongoing cross-over RCT, in which participants aged 18-25 went through 2-weeks of UPF and non-UPF diets. Before and after each diet period, participants were asked to complete a 5-trial DD questionnaire, and lnk value was calculated as the natural log of the discounting rate "k". We hypothesize subjects will have a higher increase of lnk value after the UPF diet period than after non-UPF diet period. An exploratory goal is to determine whether the lnk value can predict behaviors during an ad libitum buffet meal. We have complete DD data from n=13, partial data from n=8, and buffet meal data were collected from 18 participants who completed the study. Mixed effect model was used to assess the time (pre/post) by diet interaction on lnk value. We observed a small increase after the UPF diet ($p=0.16$), but not after the non-UPF diet. Furthermore, the regression analysis suggests that the lnk value, whether before ($p=0.64$), after ($p=0.58$) or the change across ($p=0.47$) the diet periods, does not significantly predict the ad lib buffet intake in this sample. Previous literature has suggested DD as a potential target for weight loss interventions. Our null results are likely due to the short duration of controlled feeding and the small sample size; however, we are continuing to collect data.

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Food Addiction Symptoms Predict Bmi, Ultra-Processed Fast Food Dietary Patterns, Added Sugar And Saturated Fat Intake: Evidence From Structural Equation Modeling.

Roni Aviram-Friedman¹, Or Avraham², Danit Rivkah Shahar³, Sigal Tepper²

¹Department of Nutrition Sciences, Faculty of Health Sciences, Ariel University, Ariel, Israel, ²Nutritional Sciences

The psychophysiological basis for food addiction (FA) is that FA predicts obesity. Analogous to classical addiction, this hypothesis recommends abstinence from certain foods that trigger the addiction. Previous research points to sugar, and possibly fat, as the main culprits, but this is insufficiently supported. Here, we conducted structural equation modeling to examine the relationships between FA and nutrition patterns as independent variables (IV) and food intake and BMI as dependent variables (DV). Gender's role in predicting FA and BMI was also examined. **Methods:** We assessed participants' (n=404) BMI, gender, and dietary patterns (Mediterranean; Vegan/vegetarian; Paleo/ketogenic; ultra-processed fast food). The modified Yale Food Addiction Scale (m-YFAS) and a food frequency questionnaire were conducted. The analysis focused on added sugar and saturated fat (grams). **Results:** The hypothesized model demonstrated adequate goodness-of-fit parameters (RMSEA = .06, SRMR = .05, $\chi^2(df) = 93.01(55)$, CFI = .95, TLI = .93). Six FA symptoms (YFAS 1, 7, 8, 9, 10, 11) demonstrated adequate factor loadings and were retained in the model. Food with addictive potential (AP) was predicted by saturated fat and added sugar and by FA symptoms - both directly (YFAS-S $\rightarrow$ AP) and indirectly through dietary patterns (DP) rich in ultra-processed fast food (YFAS-S $\rightarrow$ DP $\rightarrow$ AP). BMI was predicted by gender and by FA - with and without the mediating role of DP (YFAS-S $\rightarrow$ DP $\rightarrow$ BMI; YFAS-S $\rightarrow$ BMI, respectively). **Conclusions:** BMI and intake of foods rich in added sugar and saturated fat (in combination) are predicted by FA directly and indirectly (through the mediating role of ultra-processed fast-food dietary patterns). This model also supports the known role of gender in predicting FA and BMI.

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Anhedonia In Individuals With Binge Eating Or Harmful Drinking Behaviours

Taylor / N Breddy, Lindsay / P Bodell, Kendall / M Schmidt
Western University, London, ON, Canada

Aberrant reward processing has been implicated in the excessive consumption of food or alcohol. However, conflicting results exist regarding the nature of these reward processing alterations (e.g., hyper- or hypo-sensitivity) and whether alterations are specific to certain types of rewards (e.g., food, alcohol, other reward stimuli). The current study explored whether anhedonia (i.e., a construct involving reward hyposensitivity and reduced interest in activities) was related to both binge eating and harmful drinking using a between-subject design. Participants were 154 females (43 engaging in binge eating and harmful drinking, 82 engaging in binge eating only, 29 healthy volunteers) between 17 to 50 years of age ($M = 23.18$ years, $SD = 6.54$). Participants completed the Dimensional Anhedonia Rating Scale (DARS) which includes subscales assessing four dimensions of anhedonia: activities, food/drink, pastimes/hobbies, and sensory experiences. Females engaging in binge eating only demonstrated significantly greater anhedonia (i.e., lower DARS scores) on the social activities subscale compared to controls ($M = 11.37$ vs. 13.34 ; $p = .014$) and participants engaging in both binge eating and harmful drinking ($M = 13.14$; $p = .011$). They also demonstrated significantly greater anhedonia on the pastimes/hobbies subscale relative to controls ($M = 13.35$ vs. 14.86 ; $p = .022$). There were no differences between controls and individuals with both binge eating and harmful drinking on any anhedonia subscales. Findings indicate that females who engage in binge eating only might experience decreased interest in and pleasure from social and hobby-related rewards. These individuals may benefit from positive affect-focused interventions and treatment strategies.

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Valence Matters: A Meta-Analysis Of Cross-Sectional Studies Of The Relationship Between Negative And Positive Emotional Eating And Bmi

Laurence J. Nolan¹, Wesley R. Barnhart², Gabriela Diorio¹, Veronica Gallo¹, Allan Geliebter³

¹Dept. of Psychology, Wagner College, Staten Island, NY, United States, ²Dept. of Psychology, Bowling Green State University, Bowling Green, OH, United States, ³Dept. of Psychiatry, Icahn School of Medicine at St. Sinai, New York, NY, United States

Eating in the presence of negative emotion (NEE) has been associated with elevated body mass index (BMI) in a number of studies. Relatively few studies have examined eating in the presence of positive emotions (PEE), and several of them have reported that PEE is associated with lower BMI. We conducted a meta-analysis of studies that used the Emotional Appetite Questionnaire (EMAQ), which measures both PEE and NEE, and reported BMI in adults with recommended weight and overweight who were not in weight loss studies. Seventeen studies were eligible for inclusion. Age and gender were explored as potential moderators in the relationship between NEE/PEE and BMI. We found statistically significant and small mean effect sizes with random-effects models. Higher PEE (12,169 participants) was associated with lower BMI, $d = -0.067$ (95%CI: -0.107 to -0.026; $z = -3.210$, $p = .001$). Higher NEE (12,407 participants) was associated with higher BMI, $d = 0.249$ (95%CI: 0.091 to 0.351; $z = 3.453$, $p = .001$). There was significant heterogeneity in effect sizes for PEE and NEE (Q-tests for heterogeneity: $ps < .001$); however, there was no statistically significant moderation by age or gender. There was also no evidence for publication bias. A limitation was that few studies included in this analysis had measures of psychopathology or eating behaviors in common, so we were unable to examine their potential role in these relationships. The results support that NEE and PEE are different constructs. Published reports on emotional eating indicate that NEE may be associated more strongly with emotional regulation difficulties and food consumption which may explain why it is associated with higher BMI.

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Monitoring The Action Of Neuropeptides In Acute Mouse Brain Slices To Predict Anorexigenic Efficacy.

Bekir Altas¹, Nandkishor K. Mule¹, Giuseppe Bruschetta⁵, Anna Buzzanca⁵, Jonas Doerr², Daniel Lam³, Kathleen Lincoln⁵, Holger Wagner⁴, Anton Pekcec¹, Volker Mack¹

¹Department of CardioMetabolic Diseases Research, Boehringer Ingelheim Pharma GmbH & Co.KG, Biberach, Germany,

²Department of Target Discovery Sciences, Boehringer Ingelheim Pharma GmbH & Co.KG, Biberach, Germany,

³Department of Global Computational Biology and Digital Sciences, Boehringer Ingelheim Pharma GmbH & Co.KG, Biberach, Germany,

⁴Department of Medicinal Chemistry, Boehringer Ingelheim Pharma GmbH & Co.KG, Biberach, Germany,

⁵Department of CardioMetabolic Diseases Research, Boehringer Ingelheim Pharma GmbH & Co.KG, Ridgefield, CT, United States

Obesity has rapidly evolved into a major global health crisis. Etiology of obesity is predominantly attributed to an imbalance between caloric intake and energy expenditure. The physiological regulation of the energy balance is orchestrated in arcuate nucleus (Arc) of hypothalamus by two distinct neuronal populations which reciprocally modulate satiety and hunger signaling. Current therapeutic strategies employ anorexigenic peptides such as GLP-1 and GIP receptor agonists which suppress food intake by influencing these complex neural dynamics in hypothalamus. Therefore, investigating cell specific neuronal responses within the Arc is critical for profiling novel compounds and combinations thereof for developing more efficacious therapeutic strategies. Here, we have established an integrated opto-neurophysiology platform that combines functional calcium imaging and electrophysiological recordings in acute brain slices of the hypothalamus. By using calcium indicators to label neurons in the Arc, we have successfully captured distinct neuronal responses to different neuropeptides within a suitable assay window. Our platform enables sequential monitoring of individual or combined neuropeptides *in vitro*, allowing for differentiation of the individual mode of action on a neuronal network level. Moreover, we provide evidence that *in vitro* prescreening for novel combinations in our paradigm may predict *in vivo* efficacy, such as suppression of food intake and loss of body weight. Therefore, our approach not only enables the *in vitro* profiling of compounds in native hypothalamic circuitry but also enables screening of new combinations aimed at enhanced synergistic efficacy for anti-obesity treatment *in vivo*.

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Identification Preoptic Area Cells Impacted By Obesity And Diabetes In Both Male And Female Mice

Rashmita Basu^{1,2}, Sylvia Robertson¹, Connor Mahler¹, Andrew Elmendorf^{1,2}, Betty Lorentz¹, Britany App¹, Travis Johnson^{1,2}, Jonathan Flak^{1,2}

¹Indiana University School of Medicine, Indianapolis, IN, United States, ²Indiana Biosciences Research Institute, Indianapolis, IN, United States

Dynamic hypothalamic circuits protect individuals from obesity. While much is known about the main effectors in the homeostatic control of body weight, these signals are transmitted through yet to be defined efferent systems. Our goal is to develop the functional efferent circuitry from the ventromedial hypothalamic nucleus (VMN) in energy balance. VMN cells project to relatively few sites; the most prominent efferents are in the caudal regions of the preoptic area (cPOA).

Stimulating VMN^{PACAP} axonal fibers in the cPOA induces brown and beige tissue thermogenesis in both sexes of mice. Without clear targets for specialized populations, we defined the potential for excitatory (i.e. Glutamatergic) and inhibitory (i.e. GABAergic) cPOA cells by introducing hM3dq into the cPOA of knock-in vglut2 or vgat cre obese mice. Activating vgat^{cPOA} cells reduced body weight and adiposity without altering food intake, as we observed by activating VMN cells.

Activating vglut2^{cPOA} cells reduced body weight and food intake, but not adiposity. We next turned to single cell RNA sequencing to identify high-resolution and specialized cPOA populations relevant to diabetes and obesity. At this point, we have analyzed over 200,000 nuclei, the largest dataset of this region to date, from a set of mixed sex mice and identified 2 high-resolution cellular subtypes that increased in proportion in obese and glucose intolerant mice on a high fat diet. We are applying state-of-the-art deep transfer learning approaches to identify obesity and diabetes risk-associated subsets of cells. Collectively, these studies are establishing new high-resolution subtypes of cells in the POA and targetable genes for these cell populations for energy balance control.

P320

Amylin Receptor Expression Profile In AgRP Neurons: Implication For Glucagon Regulation

Guillaume Bogaerts, Christina N. Boyle, Thomas A. Lutz

University of Zurich, Institute of Veterinary Physiology, Zurich, Switzerland

The pancreatic hormone amylin was previously shown to reduce nutrient-stimulated glucagon and is therefore recognized as a valuable option for diabetic patients with hyperglucagonemia. The underlying mechanism by which amylin inhibits glucagon secretion remains largely unexplored, but a direct action on pancreatic alpha-cells is unlikely. Interestingly, agouti-related peptide (AgRP) neurons, located in the arcuate nucleus of the hypothalamus (ARC), respond to peripheral signals (e.g., leptin and ghrelin) and have been linked to glucagon release in response to hypoglycemia. In addition, AgRP neurons were shown to bind and internalize the amylin agonist, salmon calcitonin. In a first step to understand whether AgRP neurons are required for amylin's glucoregulatory action, we defined the spatial distribution of amylin receptor (AMY) components within the rat ARC using RNAscope. The functional AMY requires the co-expression of the calcitonin receptor (CTR) and receptor activity modifying proteins (RAMPs 1-3). We found that AMY components are expressed in the hypothalamus; more importantly, a subset of ARC neurons co-express AgRP, CTR and RAMPs at the cellular level. RAMP3 and RAMP2 mRNA expression does not vary significantly along the anterior-posterior axis of the ARC, and nearly 50% of AgRP neurons co-express CTR and RAMPs. Furthermore, we confirmed amylin's glucagonostatic action because our first tests demonstrated that amylin consistently reduced L-arginine-induced glucagon secretion *in vivo*. We will now determine the necessity of AgRP neurons for amylin's inhibition of glucagon. This research aims to provide insights into amylin's central action and its intricate interplay with glucoregulatory hormones.

P321

Western Diet Consumption Rescues Novel Object Recognition Memory At 24 Hours In Middle-Aged Male And Female Rats.

Gabrielle R. Bonanno, Susan E. Swithers

Purdue University, West Lafayette, IN, United States

Previous studies have demonstrated that a Western diet (WD), high in both saturated fats and refined sugars, negatively impacts performance on the Novel Object Recognition (NOR) task. These studies failed to directly compare the effects of WD consumption in middle age to that of other diets following both short and long NOR delay. Therefore, we aimed to investigate the impact of consuming a WD and yogurt sweetened with sucrose, sucralose, or sucralose with maltodextrin on NOR performance in middle-aged Sprague Dawley rats. This study examined NOR performance following a short (4-minute) and long (24-hour) delay to investigate the impact of these diets on short-term retention and memory consolidation. In the first experiment, male rats were maintained on a chow diet, given unsweetened or sweetened yogurt for 17 weeks, and tested in NOR after 24 hours. In the second experiment, male and female rats were given a WD for four weeks before being tested for object memory at 4 minutes and 24 hours. Male rats on both diets showed novel object preference at 4 minutes but not at 24 hours. However, chow-diet female rats under the same conditions showed strong object memory at both 4 minutes

and 24 hours. This was unlike the WD females, who showed object memory at 24 hours but not at 4 minutes. Finally, in experiment 3, male rats were maintained on a WD for eight weeks before being tested. Again, the chow diet males showed no memory at 24 hours. However, surprisingly while the WD males did not show a preference at 4 minutes, they did show a strong object preference at 24 hours. These results suggest that compared to what has been found in short-term NOR tests, consumption of a WD may enhance the consolidation of object recognition memory in male and female middle-aged rats.

P322 **The Effect Of A 3 Week High Fat High Sugar Diet On Gabaergic Inhibition Of Nts LepR Neurons**
Rowan C Calkins, Suzanne M Appleyard
Washington State University, Pullman, WA, United States

The nucleus of the solitary tract (NTS) integrates GI signals transmitted via the vagus nerve with other inputs before relaying them throughout the CNS to modulate food intake (FI). Chronic high-fat diet (HFD) reduces the ability of cholecystokinin (CCK) to inhibit FI and activate *c-fos* in NTS neurons. However, the phenotype of NTS neurons impacted by diet is not well understood. Activation of NTS leptin receptor-expressing (LepR) neurons inhibits FI. We have previously characterized NTS LepR neuron activation by glutamatergic vagal afferents and CCK and have examined the effects of a 3-week high fat, high sugar diet (3WHFHS) on these excitatory inputs. However, some NTS neurons also receive inhibitory GABAergic inputs. Here we determined whether LepR neurons receive GABAergic inputs and if 3WHFHS alters them compared to chow fed male and female controls. NTS LepR neurons were identified using TdTomato expressed by LepR promoter-dependent Cre recombinase. Patch-clamp recordings were made in horizontal brain slices using a high chloride internal recording solution. This allows us to identify inward GABAergic Cl^- currents when excitatory post-synaptic currents (EPSCs) are blocked by glutamate receptor antagonists. Local stimulation evoked inhibitory (eIPSCs) in LepR neurons that were blocked by GABA_A antagonists. These eIPSCs have a lower success rate (~27±8%) than solitary tract-evoked glutamatergic EPSCs. 3WHFHS did not change eIPSC success rate amplitude, holding current, and input resistance; nor did it affect the frequency or amplitude of spontaneous IPSCs. We are increasing our power to determine whether there are sex differences. Overall, our data suggests that LepR neurons receive inhibitory GABAergic inputs, but that these are not altered by 3WHFHS.

P323 **Retrograde Tracing Of Hypothalamic Projections Reveals A Distinct Spatial And Transcriptional Pattern Within The Ventromedial Hypothalamus And Mammillary Nuclei**
Bernd Coester, Dylan M. Rausch, Oliver Christensen, Charlotte H. Andersen, Tune H. Pers
University of Copenhagen, Copenhagen, Denmark

Neuronal tracing has been used extensively to map communication pathways within the brain and to peripheral organs. Here, we aim to comprehensively trace multiple hypothalamic projections in parallel to provide a hypothesis-generating resource based on single-cell transcriptomics paired with projection identities in high resolution. To this end, we injected AAV2-retro into seven brain regions previously identified to receive input from the arcuate nucleus of the hypothalamus (ARC) and collected the entire medio-basal hypothalamus (MBH) for RNA sequencing. Using isolation of nuclei tagged in specific cell types (INTACT, Mo et al. 2015), we were able to enrich for MBH nuclei of traced neurons in 58 mice. A cross-sectional comparison between those individual tracings allowed us to identify cell types with specific projection targets and make predictions about their biological function. Preliminary results show distinct neuronal subpopulations that share common projection identities and can often be found grouped in anatomical locations. We were able to recapitulate published neuronal projections from subregions of the hypothalamus to the periaqueductal grey (PAG) and the bed nucleus of the stria terminalis (BNST) in detail. Particularly, the ventromedial hypothalamus (VMH) and mammillary nuclei (MMN) demonstrate very distinct and strong outgoing projections. We then used spatial transcriptomics with unilateral, pairwise tracing of two target regions simultaneously as a proof of concept for the specificity of the tracing method. Together, this demonstrates the potential of our resource to predict new biological functions of hypothalamic neurons without a prior restriction to a specific field of interest.

P324 **Branched-Chain Amino Acids Acutely Increase Hedonics For Sucrose**
Fereshteh Dehghani, Andrew Shin
Texas Tech University, Lubbock, TX, United States

Overconsumption of palatable food is a major contributor to the recent spike in obesity prevalence. Circulating levels of branched-chain amino acids (BCAAs) are observed in both human and animal models of obesity and type 2 diabetes. Low protein and/or BCAA-restricted diets have shown to induce the expression of a hepatokine called fibroblast growth factor (FGF21), which negatively regulates simple sugar intake and sweet preference in mice. Whether or not BCAAs can alter reward functions to increase preference for palatable foods and the role of FGF21 in this process have not been explored. To test this, 8-week-old male C57Bl/6 mice were assigned to two weight-matched groups to receive intraperitoneal injections of either saline or BCAAs (225 mM) twice a day for 7 consecutive days. Before and after intervention, their 10% sucrose intake was measured for two days. Following the completion of the study, mice were sacrificed for plasma and tissue collection. Daily body weight and food intake were measured throughout the study. Plasma BCAA levels were higher in BCAA-injected group compared to saline-injected group as expected. While sucrose intake was identical between groups at baseline, BCAA treatment increased sucrose intake that was independent of body weight, food intake, or blood glucose. This was associated with lower plasma FGF21 in BCAA group compared to saline group. Our findings suggest that a short-term supplementation of BCAAs may promote indulgence in palatable sucrose solution, and this may be potentially related to the reduction in plasma FGF21 levels. Determining the long-term effects of BCAAs on sucrose preference and FGF21 as a possible mediator is warranted. Our study sheds light on the novel role of BCAAs in food reward.

P325 **Evidence Of An Association Between Dacc Glutamate Modulation During Top-Down Inhibitory Control And Weight Loss Ability In Individuals With Obesity Using ¹H Fmrs**

Jillian M. Eichstaedt¹, Rachel Sochocki¹, Dalal Khatib¹, Nicole Miller², Vaibhav A. Diwadkar¹, Paul Burghardt¹, Amy Rothberg², Jeffrey A. Stanley¹

¹Wayne State University, Detroit, MI, United States, ²University of Michigan, Ann Arbor, MI, United States

Poor inhibitory control and its association to weight loss maintenance is poorly understood. The dorsal anterior cingulate cortex (dACC) is central to inhibitory control, driven by the interplay of glutamatergic/GABAergic neurotransmission. ¹H fMRS can assess steady-state changes in glutamate driven by task condition, illuminating neurobiological mechanisms. The purpose was to investigate differences in dACC glutamate modulation during inhibitory control with/without food cues and its association with weight loss. ¹H fMRS during a visually-guided motor tapping task with 4 inhibitory control conditions and a baseline condition (Checkerboard) were collected from the dACC in 13 individuals with obesity following a clinical weight loss program (WLP). Task conditions included "Non-Selective" (motor response to 100% of trials) and "Selective" (withholding 'prepotent' responses on 20% of trials - involving both motor control and inhibition) modes; both applied with Non-Food only (Squares) and Food/Non-Food stimuli. Glutamate modulation relative to baseline was tested across stimulus-type conditions (Squares vs. Food/Non-Food) using a repeated measures GEE approach (SAS GENMOD). The task condition term was not significant ($\chi^2=3.99, p=0.136$), however, post-hoc analyses demonstrated increased glutamate during Squares ($z=-2.25, p=0.025$), but not during Food/Non-Food ($z=-1.55, p=0.122$), compared to the baseline condition. A trending correlation was observed between decreasing dACC glutamate modulation (Selective mode, Food/Non-Food) and less weight loss during the WLP [$R^2=0.274, F(1,11)=4.15, p=0.066$]. Results provide initial support that food-cues may impact inhibitory control ability and predict one's long-term inability to lose weight.

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Gaba Receptor Agonist Injected Into The Lateral Hypothalamus Suppresses Feeding Induced By The Lateral Septum

Ivett Gabriella, Vandana Nambiar, Chlinton Kuang, Aneerudh Venkatraghavan, Amandeep Sahrawat, Glenn B. Stanley
University of California, Riverside, Riverside, CA, United States

Over 40% of U.S. adults suffer from obesity or overweight, making it vital to identify the brain processes behind overeating. Past studies have shown that the septo-hypothalamic circuit involving the Lateral Septum (LS) and the Lateral Hypothalamus (LH) are anatomically and functionally connected. Yet, the functional hierarchy of these connections, particularly those involving GABA receptors in the regulation of feeding, has not been thoroughly examined. Adult male rats with chronic cannulas in the LS and the LH were administered a GABA agonist (muscimol; 0.3µg / 0.3µl) and an antagonist (picrotoxin 0.1µg / 0.3µl) to elicit contrasting responses - inhibiting feeding in one area while stimulating it in the other. The data was assessed by a 2-way repeated measures ANOVA. Results showed that feeding elicited by a unilateral muscimol injection in the LS was markedly suppressed by bilateral administration of muscimol into the LH ($n = 13$; main effect: $F_{(1,34,11)} = 8.93, p < 0.01, \eta_p^2 = 0.43$). Post hoc analysis revealed that the mean difference in food intake was $8.8 \pm 3.1g$ ($p = 0.04$) during the first hour, $9.6 \pm 2.9g$ ($p = 0.02$) during the second hour, and $9.9 \pm 2.9g$ ($p = 0.02$) during the third hour between "LS-induced" and "LS-induced while LH-suppressed" food intake. In contrast, feeding induced by unilateral LH picrotoxin injection was not suppressed by a bilateral picrotoxin injection into the LS ($n = 11$). Our results suggest that the signals from the LH override signals initiated in the LS, placing it downstream from the LS and establishing its dominant role within the septohypothalamic circuit. Given the global rise in overweight and obesity rates, this research could offer insight into a potential intervention target.

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A Microstructural Analysis Of Sucrose Licking In Glucagon Gene Knockdown (Gcg-Kd) Rats

Inge E Guerrero, Ginger D Blonde, Linda Rinaman, Alan C Spector
Department of Psychology and Program in Neuroscience, Florida State University, Tallahassee, FL, United States

Levels of glucagon-like peptide 1 (and presumably other *Gcg*-encoded products) are reduced in a homozygous *Gcg-Cre* rat model (*Gcg-KD*; 10.1016/j.molmet.2022.101631). To reveal the behavioral impact of *Gcg-KD* on sucrose intake and its underlying licking microstructure, we gave fasted or non-fasted male and female *Gcg-KD* and wildtype (WT) control rats ($N=6-8/\text{sex/genotype}$) 60-min access to 4% or 24% sucrose solution using a within-subjects nested crossover design. Compared to WT controls, female *Gcg-KD* rats drank more of both 4% and 24% sucrose when fasted and more 4% sucrose when non-fasted in the first meal before a ≥ 5 -min pause. In males, *Gcg-KD* rats overall drank more than WT during meals especially for 4% sucrose when fasted. Although the initial 1-min lick rate was significantly lower for *Gcg-KD* vs. WT males, it was only at 4% sucrose and only while fasted and did not differ between genotypes for females; the first licking burst size (≥ 3 -s pause) did not differ between genotypes for either sex. These early meal measures suggest that *Gcg-KD* does not alter the palatability of sucrose in any major way. Likewise, average burst size did not differ significantly between genotypes in either sex. Rather, increased total sucrose licking in *Gcg-KD* rats was due to a significantly higher number of lick bursts in females, and in fasted males for 4% sucrose. Collectively, these results suggest that *Gcg-KD* amplifies sucrose intake primarily by altering processes governing appetitive vs. consummatory aspects of motivated licking, especially in females. The sex differences are worthy of further investigation. Microstructural analysis of licking of diverse nutrient stimuli under various physiological states could help reveal the behavioral consequences of permanent *Gcg-KD*.

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Obesogenic Diets Differentially Alter Anxiety-Like Behavior And Dopamine Antagonist Control Of Food Intake In Female Mice

Emerson Hansard, Ana Carney, Deborah Kim, Janet Suarez, Kaylee Zhang, Wambura C. Fobbs
Swarthmore College, Swarthmore, PA, United States

Obesity is a disorder that is driven by chronic overconsumption and is correlated with various psychiatric and neurobiological features, including increased anxiety and altered dopamine system functioning. The nature and directionality of the relationship between obesity and anxiety remains unclear, with past rodent studies suggesting it could depend on the composition of high-calorie diets used to model obesity, the duration of high-calorie diet exposure, the sex of the animals, etc. Thus, we set out to test whether two different high-calorie diets (a high-fat diet, HFD, and a western diet, WD) differentially modulate anxiety-like behavior at two time points in female mice. When HFD-fed and WD-fed mice were tested on an open field test after 6 weeks of diet exposure, only the HFD-fed mice exhibited increased anxiety-like behavior relative to their weight-matched, chow-fed controls. We also tested the mice at 15 weeks to see if the difference remained. Additionally, because past research showed that long-term consumption of obesogenic diets can block the ability of the dopamine D1 antagonist SCH23390 to control intake, we assessed whether intake effects of SCH23390 were blocked in our HFD-fed and WD-fed mice after 13 weeks of exposure. As expected, the effects observed in the chow-fed controls were not observed in the HFD-fed nor WD-fed mice, with some differences. Overall, the data suggests that the nature of the relationship between obesity and anxiety depends on the composition of the high-calorie diet used to model obesity.

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Primate Amygdala Neurons Signal Oral-Sensory And Nutrient Properties Of Predicted Food Rewards In Value-Based Decisions

Fei-Yang Huang, Fabian Grabenhorst

Department of Experimental Psychology, University of Oxford, Oxford, United Kingdom

Nutrients and oral-sensory food qualities influence the subjective valuation of food. Recent studies have shown that monkeys prefer sugar- and fat-rich foods, consistent with integrating nutrient and oral-sensory properties into economic values to guide choice (Huang et al., 2021) and reinforcement learning (Huang & Grabenhorst, 2023). However, it is unclear how amygdala neurons, which encode subjective values during economic choice (Grabenhorst et al., 2012, Jezzini & Padoa-Schioppa, 2020), process nutrients and oral-sensory food attributes to infer subjective values of distinct food rewards. Here, we recorded the activity of 208 amygdala neurons from two adult male rhesus macaques (*Macaca mulatta*) while they repeatedly chose from eight liquid rewards that varied in nutrients (fat, sugar) and oral-sensory properties (viscosity, sliding friction). In each trial, two visual cues, each indicating one of the eight rewards, were sequentially presented to the monkeys, followed by a touch choice to obtain the chosen reward. Mixed-effects logistic regression ($n = 18,704$ and $22,170$ choices from monkey Ya and Ym) revealed subjective but stable preferences for fat and sugar content in both monkeys. Consistent with previous results (Huang et al., 2021, PNAS), oral-texture properties mediated the fat preference in food choice. Apart from encoding the subjective values of offered options (offer value), significant proportions of amygdala neurons also signaled nutrient and oral-sensory properties of the predicted rewards. Our findings suggest that amygdala neurons encode both nutrient and oral-sensory food properties and their integrated values, providing essential neuronal substrates for constructing subjective values to guide food choice.

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Lateral Hypothalamic Area Neurons Expressing Neurotensin Alleviate Comorbid Obesity-Pain

Rabail Khan, Hope Bemi, Raluca Bugescu, Geoffroy Laume, Gina Leininger

Michigan State University, East Lansing, MI, United States

Chronic pain and obesity frequently occur together. An ideal therapy would alleviate pain without weight gain, and most optimally, could promote weight loss. The neuropeptide neurotensin (Nts) is implicated in reducing weight and pain, but the endogenous mechanisms underlying this physiology were unknown. We previously showed that activating lateral hypothalamic area neurons expressing Nts (LHA^{Nts} neurons) suppresses feeding and promotes weight loss. Here we hypothesized that activating LHA^{Nts} neurons can also alleviate comorbid obesity pain. To test this, we injected normal weight and diet-induced obese (DIO) *Nts^{Cre}* mice in the LHA with AAVs to Cre-dependently express either mCherry (Control) or excitatory Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) in LHA^{Nts} neurons, permitting their activation after treatment with the DREADD ligand clozapine N-oxide (CNO, 0.3mg/kg, *i.p.*). Activating LHA^{Nts} neurons had no effect on thermal pain responses in DIO mice. By contrast, obesity-induced pain hypersensitivity was completely reversed by CNO-mediated activation of LHA^{Nts} neurons compared to VEH control. In DIO mice treated with complete Freund's adjuvant (which induces inflammatory pain), activating LHA^{Nts} neurons also relieved pain hypersensitivity. However, pretreatment with the brain permeable Nts receptor pan-antagonist SR142948 (1mg/kg, *i.p.*, 30 min before VEH/CNO) blocked CNO-mediated analgesia, indicating that LHA^{Nts} neurons alleviate chronic pain in an Nts-dependent manner. Furthermore, Nts deletion from the LHA by injecting AAV-Cre into the LHA of *Nts^{flox/flox}* mice further exacerbated hyperalgesia in DIO mice compared to normal weight mice. Taken together these data suggest that augmenting signaling via LHA^{Nts} neurons may be a common actionable target to treat comorbid obesity pain.

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Improvements In Exercise Performance Are Mediated By Sf1-Expressing Neurons In The Ventromedial Hypothalamus.

Morgan Kindel, Ryan Post, Jamie Carty, Nitsan Goldstein, Rachael Villari, Lukas Richie, Manmeet Rai, Hallie Kern, J. Nicholas Betley

Department of Biology, University of Pennsylvania, Philadelphia, PA, United States

Physical exercise is one of the most effective lifestyle practices in preventing metabolic, neurological, and psychiatric diseases. However, the neural mechanisms underlying these effects are unknown. The ventromedial hypothalamus (VMH) maintains energy balance by controlling components of energy metabolism. The expression of steroidogenic factor 1 (SF1), which is necessary for the development of VMH neurons, is important for endurance capacity and exercise-induced metabolic adaptations (Fujikawa et al., 2016). Thus, we sought to explore the physiology and function of VMH^{SF1} neurons during exercise. We find that activity of VMH^{SF1} neurons increases following exercise. This activity is amplified by repeated exercise training. Importantly, augmenting this activity leads to an increased exercise capacity. These findings suggest that exercise increases VMH^{SF1} neural activity and that this activity mediates metabolic and physiological adaptations that lead to increased physical fitness.

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Astrocytic And Neural Metabolic Changes Accompanying Western Diet-Induced Hippocampal DysfunctionLaura Loera-Lopez^{1,2}, Magen Lord², Jun-Won Heo³, Steven Sloan⁴, Jarrod Call^{1,3}, Emily Noble^{1,2}¹Neuroscience Graduate Program, Athens, GA, United States, ²Department of Nutritional Sciences, Athens, GA, United States, ³Department of Physiology and Pharmacology, Athens, GA, United States, ⁴Emory School of Medicine, Atlanta, GA, United States

¹Neuroscience Graduate Program, Athens, GA, United States, ²Department of Nutritional Sciences, Athens, GA, United States, ³Department of Physiology and Pharmacology, Athens, GA, United States, ⁴Emory School of Medicine, Atlanta, GA, United States

A Western diet (WD), high in saturated fats and added sugars, impairs the function of the hippocampus, a brain region important for learning and memory. While WD-induced impairments have been extensively reported in both humans and rodent models, the mechanisms by which a WD negatively impact hippocampal function remain unclear. Therefore, to

investigate the mechanisms by which a WD impact hippocampal function, we utilized a cell-type specific RNA sequencing approach to determine differentially expressed genes in both neurons and astrocytes of C57BL/6 mice fed a chow or a WD (60% kcal from fat with 11% high fructose corn syrup solution) for eight weeks. WD-induced behavioral impairments were confirmed in our model using a hippocampal-dependent Novel Location Recognition task. RNA sequencing and GO pathways analyses of hippocampal astrocytes revealed a reduction in gene expression of inflammatory pathways, but an increase in glycolytic pathways in WD-fed animals. To determine the morphology associated with this response, termed “astrocyte reactivity”, we utilized immunohistochemistry targeting glial fibrillary acidic protein (GFAP) and observed an increase in density, branch length, and number of GFAP positive signal in WD-fed animals. Changes in astrocytes were accompanied by impaired mitochondrial metabolism in hippocampal neurons with reduced gene expression of mtDNA protein encoding genes. Taken together, these findings suggest that consuming a WD has a profound metabolic impact on hippocampal cellular metabolism. Ongoing experiments are exploring whether these metabolic changes are mechanistically linked with WD-induced cognitive dysfunction.

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Peripheral Administration Of Amylin Changes The Connectivity Between The Hippocampus And Other Brain Areas In Mice

Giulia Mazzini¹, Irmak Gezginer^{2,3}, Christelle Le Foll¹, Diana Kindler², Daniel Razansky^{2,3}, Thomas A. Lutz¹

¹Institute of Veterinary Physiology, Vetsuisse Faculty, University of Zurich, Zurich, Switzerland, ²Institute for Biomedical Engineering and Institute of Pharmacology and Toxicology, Faculty of Medicine, University of Zurich, Zurich, Switzerland,

³Institute for Biomedical Engineering, Department of Information Technology and Electrical Engineering, ETH , Zurich, Switzerland

Amylin is a physiologically relevant hormone co-secreted with insulin by pancreatic β -cells in response to a nutrient stimulus, acting as a satiation signal. Amylin analogues have emerged as a promising avenue for obesity and diabetes management. Amylin exerts its effects by interacting with specific receptors located in different parts of the brain. Our laboratory has provided extensive mapping of amylin's action on eating behavior in rodents in multiple fore- and hindbrain areas. Recent studies highlighted a strong signal elicited by amylin in the hippocampus, known to play a critical role in memory. In this study, we used resting-state functional Magnetic Resonance Imaging (rs-fMRI) to test the effect of amylin (500 μ g/kg) and its long-acting receptor agonist salmon calcitonin (sCT; 10 μ g/kg) in the hippocampus. We quantified brain connectivity patterns following their peripheral injection in anesthetized wild-type (WT) mice compared to a genetically modified mouse model lacking amylin specific receptor components (RAMP 1/3 KO). Notably, in WT mice, both amylin and sCT induced marked changes in connectivity patterns involving the hippocampus. These changes were largely absent in the KO mice, indicating a specific action of amylin and sCT through amylin receptors in this brain region. Further, we showed that c-Fos expression in the hippocampus is higher in sCT-injected mice compared to vehicle-injected mice. Behavioral experiments in mice based on spatial memory tasks with and without food cues functionally complete this study. These progresses will potentially take us a step closer to unlock the full therapeutic potential of amylin analogues for a wide range of clinical conditions, thereby addressing the current lack of effective treatment options.

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Dissecting Medial Prefrontal Cortex Neuronal Ensemble Dynamics Across Contingent Food-Seeking Behavior

Sierra N Miller, Carine Lampert, Cesar Acevedo, Briana L Machen, Sheila Subbiah, Lauren E Assaf, Julia C Tucker, Morris R Jackson, Lucas Pozzo-Miller, B. Sofia Beas
University of Alabama at Birmingham, Birmingham, AL, United States

Misalignment between homeostatic energy needs and motivation for food consumption are thought to underly disorders that drive both over- and under-eating. The medial prefrontal cortex (mPFC) is a brain region that plays an important role on motivated behaviors and is known to modulate food intake and food reward valuation (Land, et. al., 2014; Warthen, et. al., 2016). However, how mPFC neuronal ensembles adapt with changes in energy state and food-reward types is still not fully understood. To address this, we use single-cell calcium imaging to characterize the activity of mPFC neurons while mice perform trials in a foraging task. Once mice were trained on the task (n=4), different trial contingencies were manipulated. We first aimed to determine how mPFC neuronal ensembles respond during distinct task events like food-approach versus feeding. For this, we utilized three different clustering methods: 1) Standard approach (Patel, et. al., 2022); 2) Unsupervised machine learning using K-means clustering with dynamic time warping (DTW) (Kinnunen, et. al., 2021); and 3) Deep machine learning using DTW-Self Organized Maps (Li, et. al., 2021). Each method resulted in differential clustering of neuronal activity. Then, to determine the effects of manipulating task contingencies, we will use a novel statistical framework based on functional linear mixed models (FLMM) (Loewinger, et. al., 2024 *preprint*; Beas, et. al., 2024). We modified and adopted the FLMM analysis to test the effects of changes in reward type (caloric and non-caloric) and energy state (hungry versus sated) on mPFC cells activity dynamics. Our work contributes highly detailed characterization of mPFC dynamics across different conditions that influence motivated food-seeking behavior.

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The Gut-Brain Vagal Axis Governs Mesolimbic Natural And Recreational Reward Dynamics

Oriane Onimus¹, Tinaig Leborgne², Faustine Arrivet³, Julien Castel¹, Philippe Faure², Nicolas Heck³, Fabio Marti³, Serge Luquet¹, Giuseppe Gangarossa¹

¹Universite Paris Cite, Paris, France, ²ESPCI, Paris, France, ³Sorbonne Universite, Paris, France

Reward-related disorders, elicited by recreational psychoactive drugs or natural rewards (food), are associated with functional, structural and long-lasting alterations of the brain dopamine (DA) reward system. Despite their intrinsic differences, drugs of abuse and palatable food lead to maladaptive modulations of the DA system that can ultimately drive

compulsive and addictive behaviours with severe health and social impacts, collectively increasing the urgent need for innovative therapeutic strategies. Visceral and interoceptive information through the vagal axis, classically described for its main role in feeding and energy homeostasis, also modulates the reward system. However, the functional underpinnings of such modulation in reward processing and associated disorders are unknown. Here, we provide evidence showing that the gut-brain vagal axis serves as an integrative lever for gating the hedonic and homeostatic effects of both natural and recreational stimuli, thereby playing a permissive role in the development of reward-based dysfunctions such as eating disorders (binge eating, obesity) and drug addiction. By taking advantage of multi-scale approaches (from integrative physiology to neuronal networks dynamics) and complementary cutting-edge techniques (neural morphology, electrophysiology, in vivo imaging) to decipher the complex role of the vagus nerve in reward/addictive behaviours, we demonstrate the existence of an extended reward system and we highlight the functional and structural adaptations of DA-neurons and dynamics within the mesolimbic system. In conclusion, we propose a novel conceptual framework that sees in the interoceptive vagal axis a major player in the development of reward dysfunctions, thus providing evidence for a new therapeutic target.

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Neuroanatomical Dissection Of The Mc3R Circuitry Controlling Energy Rheostasis

I.C Possa-Paranhos¹, J. Butts², E. Pyszka¹, C. Nelson¹, D. Cho², P. Sweeney^{1,2}

¹Department of Molecular and Integrative Physiology, University of Illinois Urbana-Champaign, Urbana, IL, United States,

²Neuroscience Program, Urbana, IL, United States

Mammals resist both acute weight loss and weight gain, although the neural circuitry mediating defense against weight change is incompletely understood. In contrast to other mutations in the leptin-melanocortin pathway, global constitutive deletion of the melanocortin-3-receptor (MC3R) results in increased weight gain following anabolic challenges and increased weight loss following anorexic challenges (i.e. impaired energy rheostasis). However, it remains unclear if this phenotype is developmental in nature or mediated by MC3R signaling in adult animals and which specific brain regions mediate the role of MC3R in energy rheostasis. Here, we utilized MC3R floxed mice, and stereotaxic viral injections of adeno-associated virus (AAV) encoding Cre-recombinase, to delete MC3R from medial basal hypothalamic (MBH) regions in adult mice. Behavioral assays were subsequently performed in these mice to test the role of whole MBH or dorsal-medial hypothalamic (DMH) deletion of MC3R in responding to orexigenic (high fat diet (HFD) administration) and anorexic stimuli (administration of the GLP1R agonist semaglutide). As observed in global MC3R KO mice, deletion of MC3R throughout the MBH or in the DMH did not alter regular chow ad libitum feeding or body weight. In contrast, deletion of MC3R throughout the MBH or only in DMH caused increased feeding and weight gain following acute HFD feeding. Conversely, deletion of MC3R in the DMH enhanced the anorexic effects of the GLP1R agonist semaglutide. These results demonstrate that MC3R mediated effects on energy rheostasis result from the loss of MC3R signaling in the hypothalamus of adult animals and indicate an important role for DMH MC3R signaling in mediating some of these effects.

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Defining The Ingestive Behavior Effects Of Endogenous Neurotensin From Lha Neurons And Their Projections

Jariel / Y Ramirez Virella^{1,2,3}, Penelope Stuart-Hurtado^{1,4}, Raluca Bugescu^{1,4}, Gina Leininger^{1,4}

¹Michigan State University, East Lansing, MI, United States, ²Neuroscience Graduate Program, East Lansing, MI, United

States, ³Department of Pharmacology & Toxicology, East Lansing, MI, United States, ⁴Department of Physiology, East Lansing, MI, United States

Obesity occurs due to excessive food consumption and a sedentary lifestyle. Development of weight loss therapies has been hindered by incomplete understanding of how the brain controls feeding and movement behaviors, and hence, how to modulate them. Experimentally activating lateral hypothalamic neurons expressing neurotensin (LHA^{Nts} neurons) transiently increases water intake and body weight, but over 24 hr it suppresses feeding and increases energy expenditure to promote weight loss. The weight reduction, but not the drinking, is believed to be mediated by Nts signaling through neurotensin receptor-1 (NtsR1), which is robustly expressed by dopamine neurons in the Ventral Tegmental Area (VTA).

Intriguingly, there may be distinct subsets of LHA^{Nts} neurons that project to different brain areas to mediate drinking vs. feeding suppression. We hypothesized that LHA^{Nts} neurons projecting to the VTA do not promote drinking but may mediate weight loss by suppressing food intake and increasing energy expenditure. To test this, we used optogenetics to activate all LHA^{Nts} neurons or only the subset that project to the VTA and compared how they modulate feeding, drinking, moving, and body weight. Our data suggest that acutely activating all LHA^{Nts} neurons drives drinking yet not weight loss, likely due to the increased water intake. Conversely, activating only the LHA^{Nts} neurons projecting to the VTA reduced feeding without invoking a drinking response. These data suggest that biasing LHA^{Nts} neuronal signaling to the VTA may be useful to support feeding restraint without undesired drinking effects. Our work begins to shed light on how distinct LHA^{Nts} neuronal projections regulate different aspects of physiology and might be leveraged to address different ingestive needs.

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Vta Projecting Nts Neurons Encode Hunger Signals Via Polysynaptic Vagal Afferent Innervation.

Caitlin R. Ritchey, David J. Rossi, James H. Peters

Washington State University, Pullman, WA, United States

Goal-oriented behaviors, including food intake, are driven by evolutionarily ancient and extensive neurocircuitry that integrates internal and external cues. The midbrain ventral tegmental area (VTA) shapes these behaviors via dense dopaminergic projections to many key forebrain areas. In addition, the VTA serves as an integrator of neural inputs from throughout the brain that modulate VTA output to inform and drive appetitive behaviors. Yet, little is known about the ascending 'bottom up' neural innervation and regulation of the VTA. The brainstem nucleus of the solitary tract (NTS) is the primary site for integration of peripheral viscerosensory and taste information and is essential for the control of food intake. Importantly, the NTS has been shown to form direct connections with the VTA, but little is known about the anatomical and neurophysiological nature of these projecting neurons or how they shape VTA output to influence appetitive feeding behaviors. Using VTA-targeted Retrobead injections, we found that the NTS forms direct monosynaptic connections with the VTA and that Retrobead labeled neurons are distributed through all levels of the NTS (rostral to caudal). Further

immunohistochemical and RNAscope analysis identified that two distinct populations of labeled neurons express tyrosine hydroxylase or glucagon-like peptide-1. Using patch-clamp electrophysiology, we found that VTA-projecting NTS neurons are largely driven by polysynaptic vagal input, have different basal synaptic properties than unlabeled neurons, and are inhibited by the satiety peptide cholecystokinin. These findings are the first step in characterizing the nature of NTS inputs to the VTA that may play a role in regulating mesolimbic dopaminergic output to control appetitive feeding responses.

P339 **Developmental Effects Of Environmental Enrichment On Solitary Binge Ethanol Consumption And Anxiety-Like Behavior**

Joshua P Sevigny^{1,2}, Sean Schrank¹, N Ika Yunus¹, Katherine R Vetter¹, Mikaela Valchinova¹, Vivek Ily¹, Oscar D Aguilar¹, Dennis R Sparta^{1,2}

¹Department of Psychology, University of Illinois Chicago, Chicago, IL, United States, ²Graduate Program in Neuroscience, University of Illinois Chicago, Chicago, IL, United States

Alcohol use disorder (AUD) affects 12 % of adults, and 3% of adolescents in the United States. Solitary drinking behavior in teens greatly increases risk of AUD in early adulthood. During the COVID-19 pandemic, solitary alcohol consumption increased dramatically demonstrating the profound effect environmental conditions can have on alcohol consumption. Environmental enrichment has been found to have highly translational impacts on both mammalian physiology and behavior, especially in the context of stress and anxiety. In adolescent mice, enrichment has been shown to transiently decrease overall alcohol consumption and anxiety-like behavior, however, it is unknown if environmental enrichment has permanent physiological and behavioral effects on solitary drinking behavior. To investigate, we applied enriched and impoverished conditions to early adolescent mice (P21-P33) and then measured solitary binge ethanol consumption in the DID model and anxiety-like behavior in open field, novel-object and elevated plus maze paradigms for three weeks post enrichment phase. Our preliminary data shows that adolescent EE decreased ethanol consumption in females but increased ethanol consumption in male mice. Furthermore, male, and female EE groups showed reduced anxiety-like responses before and after ethanol consumption. We applied the same paradigm to adult mice (>P60). In the adults, we did not find an effect of EE on isolated binge drinking, but we observed decreased anxiety-like phenotype. Future experiments will explore the neural basis of these effects. Our results support the hypothesis that specifically adolescent enrichment modulates binge ethanol consumption and anxiety-like behavior.

P340 **Zona Incerta Melanin-Concentrating Hormone-Producing Neurons Promote Consumption Of Lipids In Rats**

Keshav S Subramanian², Cindy Gu¹, Lea Decarie-Spain¹, Anna C Nourbash¹, Alicia E Kao¹, Molly E Klug¹, Arun A Ahuja¹, Kara Mcburnett¹, Kristen N Donohue¹, Alyssa M Cortella¹, Sarah J Terrill¹, Denis Burdakov³, Lindsey A Schier^{1,2}, Scott E Kanoski^{1,2}

¹Human and Evolutionary Biology Section, Department of Biological Sciences, Dornsife College of Letters, Arts and Sciences, Los Angeles, CA, United States, ²Neuroscience Graduate Program, Los Angeles, CA, United States, ³Department of Health Sciences and Technology, Zurich, Switzerland

Melanin-concentrating hormone (MCH) is a neuropeptide that promotes excessive eating and obesity. MCH's role in food intake has thus far been evaluated using pharmacological or neuron-specific functional approaches that target all MCH neurons. However, MCH is produced in both the lateral hypothalamic area (LHA) and the zona incerta (ZI), which are adjacent regions that are differentiated both functionally and neuroanatomically. Here we employ functional imaging, chemogenetic, and behavioral approaches to elucidate the function of ZI MCH neurons, specifically. Using *in vivo* fiber photometry, results reveal that ZI MCH neuron Ca²⁺ activity increases during consumption of a high-fat diet, yet decreases during consumption of standard chow. We functionally validate these diet-specific effects under various feeding conditions using chemogenetics, revealing that ZI MCH neuron activation reliably promotes high-fat diet consumption with opposing effects on chow. To confirm whether these effects are due to macronutrient specificity vs. other differences between the diets (e.g., palatability), we reveal that ZI MCH neuron activity increases during isolated lipid consumption (4.1% corn oil emulsion) and decreases during isolated carbohydrate consumption (10% sucrose solution), and ZI MCH neuron activation increases or reduces consumption of each solution, respectively. Importantly, these results were independent of caloric-density, palatability, and thirst, as both macronutrient solutions were equicaloric and equiprefered, and ZI MCH neuron activity was not responsive to water licking. Taken together, these data support a role for ZI MCH neurons in promoting macronutrient-specific consumption of fat-dense foods.

P341 **State-Dependent Central Synaptic Regulation By Glp-1 Is Essential For Energy Homeostasis**

Le Wang¹, Rohan Savani¹, Matteo Bernabucci¹, Yi Lu¹, Ishnoor Singh², Wei Xu³, Abdelfattah El Ouaamari¹, Michael Wheeler², Harvey J. Grill⁴, Mark Rossi¹, Zhiping Pang¹

¹Rutgers University, New Brunswick, NJ, United States, ²University of Toronto, Ontario, ON, Canada, ³UT Southwestern Medical Center, Dallas, TX, United States, ⁴University of Pennsylvania, Philadelphia, PA, United States

Central nervous system (CNS) control of metabolism plays a pivotal role in maintaining energy homeostasis. Glucagon-like peptide-1 (GLP-1, encoded by *Gcg*), secreted by a distinct population of neurons located within the nucleus tractus solitarius (NTS), suppresses feeding through projections to multiple brain targets. Although GLP-1 analogs are proven clinically effective in treating type 2 diabetes and obesity, the mechanisms of GLP-1 action within the brain remain unclear. Here, we investigate the involvement of GLP-1 receptor (GLP-1R) mediated signaling in a descending circuit formed by GLP-1R neurons in the paraventricular hypothalamic nucleus (PVN^{GLP-1R}) that project to dorsal vagal complex (DVC) neurons of the brain stem in mice. PVN^{GLP-1R} neurons -to- DVC synapses release glutamate that is augmented by GLP-1 via a

presynaptic mechanism. Chemogenetic activation of PVN^{GLP-1R}-to-DVC neurons suppresses feeding. The PVNGLP-1R-to-DVC synaptic transmission is dynamically regulated by energy states. In a state of energy deficit, synaptic strength is weaker but is more profoundly augmented by GLP-1R signaling compared to an energy-replete state. In an obese state, the dynamic synaptic strength changes in the PVNGLP-1R-to-DVC descending circuit are disrupted. Blocking PVNGLP-1R-to-DVC synaptic release or ablation of GLP-1R in the presynaptic compartment increases food intake and causes obesity, elevated blood glucose, and impaired insulin sensitivity. These findings suggest that the state-dependent synaptic plasticity in this PVNGLP-1R-to-DVC descending circuit mediated by GLP-1R signaling is an essential regulator of energy homeostasis.

P342 **Stimulating Neurotensin-Expressing Neurons In The Lateral Hypothalamic Area Promotes Drinking: Is It Mediated Via Neurotensin Signaling?**

Raluca Bugescu¹, Rabail Khan^{1,2}, Alexis Boron^{3,4}, Gina Leininger^{1,2,4}

¹Michigan State University, Department of Physiology, East Lansing, MI, United States, ²Michigan State University, Neuroscience Graduate Program, East Lansing, MI, United States, ³Michigan State University, Department of Pharmacology and Toxicology, East Lansing, MI, United States, ⁴Michigan State University, Molecular, Cellular, and Integrative Physiology Graduate Program, East Lansing, MI, United States

Drinking is essential for survival, yet much remains to be understood about the mechanisms controlling this behavior. Lesioning the lateral hypothalamic area (LHA) in rodents severely inhibits their motivation to drink water, indicating the vital role of the LHA as a whole for drinking. Moreover, dehydration increases expression of the peptide Neurotensin (Nts) in the LHA, but not other brain areas. Taking these data into account, we hypothesized that LHA neurons expressing Nts (referred to as LHA^{Nts} neurons) play a critical role in promoting drinking that depends on Nts signaling via its receptors neurotensin receptor 1 (NtsR1) and/or neurotensin receptor 2 (NtsR2). To test this, we expressed excitatory Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) in LHA^{Nts} neurons of mice and treated them with vehicle (control) or the DREADD ligand CNO to activate them. Interestingly, CNO-activation of LHA^{Nts} neurons had no effect on drinking during the dark cycle but promoted voracious water intake during the light cycle. RNAScope analysis revealed that Nts expression in the LHA is lower during the light cycle (when activating LHA^{Nts} neurons can spur drinking) compared to the dark cycle (when it does not), suggesting Nts itself may not be the driver of drinking. Indeed, neither pretreatment with an NtsR2 antagonist nor a pan NtsR1/NtsR2 antagonist prior to activating LHA^{Nts} neurons diminished drinking. Taken together, these data suggest that LHA^{Nts} neuron-stimulated drinking is not regulated via Nts signaling, but instead by other transmitters released from LHA^{Nts} neurons during the light cycle. Going forward, defining the contributions of other signals in LHA^{Nts} neurons, such as CRH and GABA, may reveal how these neurons contribute to drinking behavior.

P343 **The Glucose Responsive Gliotransmitter Octadecaneuropeptide (Odn) Regulates Systemic Metabolism Through Action In The Hindbrain**

Caroline E Geisler¹, Halcyon Hu¹, Drew Belser¹, Kylie Chichura², Robert P Doyle², Matthew R Hayes¹

¹University of Pennsylvania, Philadelphia, PA, United States, ²Syracuse University, Syracuse, NY, United States

The brains' ability to sense and respond to circulating glucose is perturbed in obesity and type 2 diabetes which contributes to dysregulated long-term fuel storage. Glial cells, notably astrocytes and tanycytes, have been increasingly implicated in central glucose sensing mechanisms and synthesize the anorexigenic factor octadecaneuropeptide (ODN) in response to hyperglycemia. The dorsal vagal complex (DVC) of the hindbrain is sensitive to gut-derived and circulating nutrient satiety cues, initiates the counterregulatory response to hypoglycemia, and is densely innervated with ODN releasing tanycytes. Yet, a role of ODN in hindbrain glucose sensing mechanisms has not been established. We revealed that 4th ventricle (4V) ODN interrupts the hyperphagic and hyperglycemic response to 5-thioglucoce (5TG) induced glucoprivation, at least in part through blunting the 5TG stimulated rise in serum glucagon and free fatty acids. Similarly, 4V ODN attenuates insulin-induced hyperglucagonemia, suggesting hindbrain ODN may engage a DVC-to-pancreascircuit. Hindbrain targeted ODN also improves glucose clearance during oral glucose tolerance and insulin tolerance tests in the lean and obese state. Interestingly, 4V pharmacological antagonism of the ODN GPCR worsens insulin sensitivity and acutely elevates basal blood glucose, supporting the hypothesis that endogenous hindbrain ODN tone acts to maintain euglycemia. This work highlights ODN as a glial-to-neuronal indicator of elevated glycemic status that enhances postprandial systemic glucose disposal. Therapeutic targets of ODN signaling represent a novel strategy to improve diet-induced dysfunctions of central glucose sensing and restore peripheral responsiveness to changes in fuel status that promote whole-body energy homeostasis.

P344 **Relationship Between Habitual Low-Calorie Sweetener Consumption, Plasma Fgf21 Concentrations, And Sweetness Preferences In Adults With Obesity**

Stephanie Okoye¹, Mariel Molina-Castro², Blair Rowitz^{1,2}, M Yanina Pepino^{1,2,3}

¹Division of Nutritional Sciences University of Illinois Urbana-Champaign, URBANA, IL, United States, ²Food Science and Human Nutrition University of Illinois Urbana-Champaign, URBANA, IL, United States, ³Carle Illinois College of Medicine, URBANA, IL, United States

Since discovering the glucose-lowering effects of fibroblast growth factor 21 (FGF21) in 2005, further research uncovered the potential modulatory effect of this hepatic hormone in eating behavior, particularly for sweets. One of the research

focuses in our laboratory is to determine possible mechanisms underlying the paradoxical association of frequent low-calorie sweeteners (LCS) consumption and increased diabetes risk. Here, we investigated whether habitual consumption of LCS is associated with abnormal plasma FGF21 concentration responses to a glucose tolerance test (OGTT). In addition, we assessed whether habitual consumers of LCS (HC) reduce sugar intake in their diets (i.e., replace sugar with LCS) and evaluated whether habitual consumers differed from non-habitual consumers (NHC) in terms of sweet taste sensitivity and sweet preferences. To this aim, we studied two groups of participants with obesity; one included HC of LCS (n=34, consumed >5 diet sodas or LCS equivalent/week), and the other included NHC of LCS (n=20, consumed ≤1 diet soda or LCS equivalent/week). We measured plasma levels of FGF21 over five (5) hours post OGTT and assessed total and added sugar intake using a diet history questionnaire and sweet taste preferences using sensory techniques. We found that FGF21 responses to the OGTT, sweetness perception, and sweet preferences were similar between LCS groups (all P-values >0.1). Remarkably, habitual LCS consumers had similar total sugar intake to non-habitual LCS consumers. Our data suggest that LCS consumers are not “replacing” sugars with LCS; instead, they consume a sweeter diet. It also suggests heavy LCS consumption may not be influencing glucose metabolism via FGF21.

P345

Leptin 116-130 Reduces Demand Intensity For Sucrose Without Changes In Food Intake.

Rodrigo RamÍez-Romero¹, Yanireth JimÍnez¹, Karina Cordero¹, Rene Baudrand¹, VÍctor CortÍs¹, Bredford Kerr², Claudio PÍrez-Leighton¹

¹Pontificia Universidad CatÍlica de Chile, Santiago, Chile, ²Universidad San SebastiÍn, Santiago, Chile

Leptin is a hormone released by the white adipose tissue that reduces glycemia, food intake, and food-seeking behaviors. Leptin116-130 (Lep116-130) is a leptin fragment that reduces food intake independently of the leptin-b receptor, but whether it alters other physiological or behavioral parameters regulated by leptin remains unknown. We aimed to determine whether Lep116-130 alters glycemia and food-seeking behaviors. In the first experiment, leptin-deficient mice (*ob/ob*, n=8) and wildtype mice (WT, n=7) were injected intraperitoneally (IP) with Lep116-130 (1 mg/kg) or saline 15 minutes before analysis of chow intake or glucose tolerance test (GTT). In the second experiment, motivation for sucrose, change in body weight and cumulative food intake were measured before and after chronic delivery of Lep116-130 (n=3, 0.25 µg/hr) or vehicle (n=4) for 14 days. WT mice were tested before and 14 days after sham surgery (n=4). Motivation for sucrose was measured using a demand curve, a behavioral economic test that measures demand flexibility (α , interpreted as motivation for sucrose) and intensity (q_0 , interpreted as hedonic value of food). Acute IP administration of Lep116-130 did not change chow intake (p=0.89) or GTT AUC (p=0.8). Chronic administration of Lep116-130 did not change body weight, food intake, and α (p>0.05 for all endpoints) compared to vehicle administration in *ob/ob* or WT mice. However, it decreased the q_0 compared to vehicle-treated *ob/ob* by 107±16.2% (p=0.02), and by 109±19.3% compared to WT mice (p=0.04). Together, these data show that Lep116-130 can reduce demand intensity for sucrose without changes in food intake or body weight. These results suggest that Lep116-130 could regulate the hedonic value of food without altering energy balance.

P346

Sex Differences In High-Fat Diet Induced Dysbiosis

Morgan R. Sothen¹, Stina Borchers², Suyeun Byun¹, Doris I. Olekanma¹, Karolina P. Skibicka^{1,2}

¹The Pennsylvania State University, State College, PA, United States, ²University of Gothenburg, Gothenburg, Sweden

Chronic consumption of high-fat diet (HFD) is a potent modulator of gut microbiota. While this interaction is well established in male animal models, less is known about the impact of HF obesogenic diet on female microbiota. Considering that sex differences exist in the microbiota of lean males and females and the pathophysiology of obesity in males and females, it is likely that gut microbiota response will differ between sexes. Here we aim to investigate sex differences in the high-fat diet induced gut dysbiosis. Adult male and female rats were fed HFD or standard chow. HFD significantly increased food intake and body weight, as well as white adipose weights 6 weeks from diet initiation. Fecal samples were also collected at 6 weeks, to examine the differences in microbiota using 16S rRNA analysis. We found that alpha-diversity metrics, comparing evenness and richness of microbial species, were decreased in HFD-fed females. However, in males, HFD produced a trend to increased evenness and only marginal changes in richness. Beta diversity, an initial indication of a shift in the microbial community composition, was altered by HFD to a similar extent in both sexes, where HFD-fed males and females displayed a distinct separation from their chow-fed counterparts. Abundance of over 60 taxa was reduced and another 40 increased in females by the HFD. While the numbers of altered taxa were similar in males, the specific taxa affected were largely sex divergent. Further analysis of the cytokines and metabolites in plasma and brain was performed to determine the primary microbial drivers of each parameter per sex. Our data indicate drastic differences in the specific effects of HFD on the gut microbial community, with links to systemic and central metabolism and inflammation.

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The McLean-Stanford-Washington Lifetime Eating Disorders (Mswed) Questionnaire: Development And Piloting In Clinical Cases And Controls In Mexico

Kristin N. Javaras^{1,2}, Rocky E. Stroud^{3,4}, Beatriz Camarena-Medellín⁵, Victoria F. Franco¹, Franjo Ivankovic⁴, Benjamin M. Neale⁴, Mark J. Daly⁴

¹McLean Hospital, Belmont, MA, United States, ²Harvard Medical School, Boston, MA, United States, ³Harvard T.H. Chan School of Public Health, Boston, MA, United States, ⁴Stanley Center for Psychiatric Research, Broad Institute of MIT and Harvard, Cambridge, MA, United States, ⁵Departamento de Farmacogenética, Instituto Nacional de Psiquiatría Ramón de la Fuente Múñiz, Mexico City, Mexico

Uncovering rare genetic variants that substantially impact the risk of eating disorders (EDs), such as anorexia nervosa (AN) and bulimia nervosa (BN), can illuminate potential therapeutic targets for these disorders. However, genetic investigations require 10,000s of ED cases, precluding interview-based assessment of diagnostic status. Further, reliance on clinical diagnoses alone can result in ascertainment bias, since treatment-seeking individuals are not fully representative of those with EDs more broadly. Thus, we developed and piloted the MSWED questionnaire, which is designed to assess lifetime history of certain eating disorders, including AN and BN. It is designed to be specific rather than sensitive to ensure that most MSWED-defined cases are true cases. Similar to the Structured Clinical Interview for DSM-5 Disorders (SCID-5), the MSWED has screening questions that, if answered affirmatively, are succeeded by several follow-up questions. The screening questions assess four symptom clusters (low weight; binge eating with compensatory behavior; binge eating

without compensatory behavior; dietary restriction), and the follow-up questions are based on items from the Stanford-Washington University Eating Disorder screen. In a pilot sample of ED cases ($n = 128$, of whom 59 and 79 had clinical diagnoses of AN and BN, respectively but not mutually exclusively; female at birth = 96.9%; mean age = 25.5 years) and controls ($n = 115$; female at birth = 90.4%; mean age = 25.3 years) ascertained from ED and other medical clinics in Mexico, the MSWED's specificity with respect to clinical diagnosis was 93.5% for AN and 97.5% for BN. Based on the MSWED's excellent performance in this pilot sample, future plans include validating the MSWED against the SCID-5 in U.S. adults.

9:30 - 10:00 AM	Riverwalk A
Coffee Break	
10:30 - 12:10 PM	Ballroom III
Symposium 4: Weight gain and weight loss influences on the brain	

Chair(s): Matt Howe

10:30

Obesity, Insulin Resistance, Cognitive Impairment, And Alzheimer-Type Neurodegeneration: A Preventable Global Crisis

Suzanne de la Monte^{1,2,3}, Vania Kasper^{2,3}, Ming Tong^{1,2}

¹Rhode Island Hospital-Brown Medical School, Providence, RI, United States, ²Alpert Medical School of Brown University, Providence, RI, United States, ³Hasbro Children's Hospital, Providence, RI, United States

Insulin resistance causes cognitive impairment and neurodegeneration, including Alzheimer's (AD), which has risen with obesity and diabetes. Soaring costs and declining quality of life urge us to reverse these trends by considering the roles of diet, exposure, and pathogenic initiators. Preclinical models examined effects of diet-induced obesity (DIO) and cofactor nitrosamine preservative exposures on neurodegeneration. Brain, CSF, and serum from humans with normal aging, MCI, or AD were examined for metabolic and inflammatory indices of neurodegeneration and insulin-related metabolic dysfunction. Obese children were evaluated for cognitive impairment and insulin resistance. In rats, DIO caused MCI and early changes of AD accompanied by brain insulin resistance and oxidative stress. DIO plus nitrosamines worsened cognitive function, brain atrophy, and AD pathology. In humans, MCI and AD were associated with abnormal CSF and serum markers of insulin resistance-linked metabolic dysfunction, including deficits in incretin expression; the effects were greater in AD than MCI, corresponding with severity of neurodegeneration. Childhood obesity associated with hepatic and systemic insulin resistance, hepatic steatosis, and increased abdominal circumference was associated with impaired performance on executive function, working memory, and attention tests. Insulin resistance with dysregulated metabolism adversely impacts brain structure and function across the lifespan and is the blueprint for cognitive decline and neurodegeneration. Epidemiological rate shifts in cognitive impairment and AD are likely mediated by combined excesses in caloric consumption and chronic exposures to processed foods containing nitrate/nitrite preservatives, which as a society, we could halt.

10:55

Impact Of Gastric Bypass Surgery On Gut-Brain Communication (Supported By The Ssib International Foundational Fund Given In Memory Of Drs. Jacques Le Magnen (France), Anton Steffens (The Netherlands), Jacob Steiner (Israel), Steven Cooper (The United Kingdom))

Mohammed Hankir

Department of Veterinary Physiology, University of Zurich , Zurich , Switzerland

Obesity is associated with impaired neuronal function at various levels of the CNS, including in homeostatic feeding centres in the hypothalamus and reward feeding centres in the striatum. For my talk, I will draw upon the clinical and preclinical work on how gastric bypass surgery, which remains the mainstay treatment for severe obesity, reverses some of these central deficits through complex changes in gut-brain communication to ultimately steer feeding behaviour in the healthier direction. Finally, I will present some preliminary data on how gastric bypass surgery reprograms the transcriptome throughout the entire neuraxis from the hindbrain through to the prefrontal cortex. It is hoped that these findings will provide useful insight into how bariatric surgery exerts such a strong hold on various aspects of the feeding process.

11:20

Exploring Brain Changes After Bariatric Surgery: Insights From Prospective Studies

Andreanne Michaud^{1,2,3}

¹Ecole de nutrition, Université Laval, Quebec, QC, Canada, ²Centre de recherche de l'Institut universitaire de cardiologie et de pneumologie de Quebec, Université Laval, Quebec, QC, Canada, ³Centre NUTRISS, Institut sur la Nutrition et les Aliments Fonctionnels, Université Laval, Quebec, QC, Canada

Obesity is associated with diminished cerebral grey and white matter integrity, particularly in fronto-temporal regions, which may substantially mediate the emerging links between obesity and accelerated cognitive decline. Bariatric surgery, the most effective treatment modality for severe obesity, represents a unique model to examine the impact of marked weight loss and cardiometabolic improvements on brain structure and function in a prospective setting. Over the past decade, several studies have reported significant changes in brain structure and function following weight loss induced by bariatric surgery. Recent work from our group demonstrated widespread increases in white matter and grey matter densities, as well as neural activity at 4, 12 and 24 months following bariatric surgery, suggesting a global effect of surgery on brain status. To further investigate these findings, we conducted a study evaluating the impact of weight loss and cardiometabolic improvements following bariatric surgery on a biomarker of brain health, measured by changes in estimated brain age. Our results showed a significant improvement in brain health, indicated by a decrease of 2.9 and 5.6 years in estimated brain age 12 and 24 months post-surgery compared to baseline. This decrease in estimated brain age following bariatric surgery was significantly associated with the degree of weight loss and concomitant improvement in cardiometabolic factors. Together, these findings suggest that obesity-related brain health abnormalities might be reversed by means of significant and sustained weight loss, along with widespread improvements in cardiometabolic alterations.

11:45

Neurocognitive Consequences Of Adult Obesity

Filip Morys

Montreal Neurological Institute, McGill University, Montreal, QC, Canada

Obesity intersects with brain health. Neurocognitive traits may lead to weight gain and long-term obesity causes brain atrophy. In a series of studies we found that neurocognitive correlates of obesity change across the lifespan. In children, cortical changes and impulsivity are associated with weight gain and obesity. In turn, chronic obesity is associated with comorbidities such as inflammation, hypertension, dyslipidemia, or type II diabetes. In older adults, these can lead to grey matter atrophy, and cognitive decline. Genetic and neurochemical analyses point to an involvement of inflammatory and mitochondrial metabolic processes and several neurotransmitter systems in this phenomenon. Importantly, mechanisms underlying obesity-related neurodegeneration seem to be different from the ones involved in typical neurodegenerative diseases and involve predominantly cerebrovascular disease as opposed to accumulation of proteins such as amyloid- β or tau. Our findings emphasise the critical role of interventions aimed at weight loss and obesity prevention in improving brain health.

Oral Session 6: Just Can't Get Enough

Chair(s): Jennifer Temple

10:30

Mechanisms Underlying Cannabinoid-Induced HyperphagiaMagen N. Lord¹, Grace C. Madu¹, Mai O. Spaulding¹, Jessica R. Hoffman², Emily E. Noble¹¹Dept. of Nutritional Sciences, University of Georgia, Athens, GA, United States, ²Dept. of Physiology and Pharmacology, University of Georgia, Athens, GA, United States

Cannabis and cannabinoid use has increased over the last decade coinciding with the legalization of marijuana in several states. Cannabinoids increase eating behavior via the central cannabinoid receptor (CBR), but the neurological and behavioral mechanisms are not fully understood. To investigate the mechanisms by which cannabinoids increase food intake, we developed a novel delivery method for administering CBR agonists to rodents modeling a common method of human cannabinoid consumption: gelatin-based edibles. Dual CBR agonist (CP55940) containing edibles elevated standard chow intake in Wistar rats when compared to a vehicle edible. Interestingly, we found a sex difference in cannabinoid-induced hyperphagia driven by increased meal size in females and increased meal frequency in males. We further tested the impact of edible CP55940 on impulsive eating behavior and motivated responding for food in female rats using the differential reinforcement of low rates of responding and progressive ratio tasks, respectively. Administration of edible CP55940 increased impulsive responding for sucrose but had no impact on motivated responding. Surprisingly, edible CP55940 increased spontaneous activity in female rats in both fed and fasted conditions. Given that orexins increase both food intake and spontaneous activity, we investigated whether orexin neurons of the lateral hypothalamus elevated c-FOS expression following a hyperphagic dose of edible CP55940, however we observed no group differences in orexin c-FOS activity in the fed or fasted condition. Taken together, these data show edible CP55940 increases food intake in a surprising sex specific pattern and increases impulsive action in females without affecting food motivated responding.

10:45

Macronutrient-Specific Signatures Of P_{ost}-Ingestive Striatal Dopamine Dynamics

Tu'ng T. Bu'i, Alec E. Hartle, Caroline R. Sallee, William M. Howe

School of Neuroscience, Virginia Polytechnic Institute and State University, Blacksburg, VA, United States

Emerging evidence suggests that the macronutrient composition of a food modulates its reward value, and that anatomically distinct circuits relay information about fat and carbohydrates in foods to midbrain dopamine (DA) cells. We hypothesized that the ability of different macronutrients and combinations to modify food reward stems from their unique effects on DA release patterns in the brain reward circuits, in particular the striatum. To test this hypothesis, C57 mice (n=6) were implanted with an intra-gastric catheter, along with the fluorescent DA sensor dLight1.1 to measure sub-second DA release dynamics in the striatum. Each mouse was infused with a single calorie of fat (intralipid), sucrose, a combination of the two, or a PBS vehicle while spontaneous DA release was recorded in the dorsal striatum of freely moving mice. We quantified spontaneous DA release frequency and amplitude prior, during, and after intra-gastric infusions. Preliminary analyses revealed that relative to vehicle, infusion of nutrients into the gut reduced the frequency of ongoing spontaneous DA release. The rate of such release rebounded above pre-infusion baseline levels in the 20 minutes after infusion. We further noted an increase in the amplitude of spontaneous release events in this rebound period, an effect that was greatest following lipid infusion. Our ongoing experiments assess the regional specificity of these changes by monitoring post-ingestive modulation of spontaneous DA release in the nucleus accumbens. Our data suggest that activation of ascending pathways from the gut to the midbrain alter the patterning of spontaneous DA release in a macronutrient-specific manner. These effects could contribute to the ability of macronutrient composition to modify food reward.

11:00

Insulin Resistance And Sugar Reinforcement In People With ObesityLeonard Epstein¹, Ashfique Rizwan¹, Sameeha Rasheed¹, Warren Bickel², Husam Ghanim¹¹University at Buffalo Jacobs School of Medicine and Biomedical Sciences, Buffalo, NY, United States, ²Virginia Tech Carillion School of Medicine, Roanoke, VA, United States, ³University at Buffalo Jacobs School of Medicine and Biomedical Sciences, Buffalo, NY, United States

The development of type 2 diabetes (T2D) is related to insulin resistance (IR), and most people with prediabetes who develop T2D are obese. A goal for people with prediabetes and obesity is to reduce energy intake and intake of sugar and high glycemic index (GI) carbohydrates. Research suggests sugar and high GI foods are highly reinforcing and activate brain reward centers. If IR increases the reinforcing value of high GI foods, it may be challenging for people with IR to reduce intake of high GI foods. This talk describes results of two studies designed to assess the relationship between IR and the choice and reinforcing value of sugar-sweetened foods. Thirty-one people with obesity and varying levels of IR (range 0.6-11.6) were provided sugar or monkfruit-sweetened yogurt to consume in a within-subject design using a flavor-color conditioning paradigm in which novel yogurt flavors and colors were sweetened with sugar or monkfruit that differentially

impact blood glucose but were perceived as equally sweet. **Study 1** showed participants consumed more ($p=0.009$) sugar than monkfruit-sweetened yogurt, which was related to IR ($r=0.64$, $p=0.019$), insulin ($r=0.58$, $p=0.007$) and glucose ($r=0.56$, $p=0.048$). **Study 2** showed IR ($r=.62$, $p=0.006$) and insulin ($r=.51$, $p=0.03$) were related to the reinforcing value of sugar-sweetened yogurt. People with greater IR and greater blood glucose changes to a glucose challenge responded the most for sugar-sweetened yogurt ($p=0.02$). Insulin resistance is associated with preference for sugar-sweetened foods in participants with obesity, which may make it hard to make dietary changes. Research is needed to assess whether treatments that improve insulin resistance also change the reinforcing value of sugar-sweetened or high glycemic index foods.

11:15

Food Reinforcement As A Predictor For Child Dietary Changes During A Test Meal After A Restrictive Period.

Hannah Kolpack¹, Lori Hatzinger^{1,2}, Jennifer L. Temple¹, Katherine N. Balantekin¹

¹University at Buffalo, Buffalo, NY, United States, ²University of Southern California

The aim of the study was to examine how weight status impacts the relationships among the reinforcing value of food (RRV) and dietary intake during a test meal at baseline and after a restriction and structured feeding period. 68 participants, 8–11 years old [54% boys], completed four visits. On visit 1, height/weight were measured and RRV of a HED food was assessed. At visits 2 (control meal; CONT), 3, and 4, participants ate at an identical test meal with 25 foods and 3 drinks. Between visits 2-3 and 3-4, participants completed two weeks of restriction (R) of their RRV food and two weeks of structured intake of their RRV food (were given 8 portions; SI), with order of conditions counterbalanced. In order to assess the impact of food restriction on intake relative to the other two conditions, change scores were created by subtracting energy and macronutrient intake of the CONT and SI from the intake after R. Linear regression was used to examine if RRV predicted changes in energy and macronutrient intake. For the total sample and for participants with healthy weight, RRV did not predict energy or macronutrient intake. Relative to CONT, in participants with OW/OB, RRV positively predicted marginally larger intake of CHO ($p = .058$) and significantly larger intake of protein ($p = .006$) at the R test meal. Relative to SI, participants with OW/OB had a significantly higher total calorie intake ($p = .037$), CHO ($p = .033$), and fat ($p = .016$) at the R test meal. In sum, these data suggest that RRV could indicate how a child with OW/OB would react under restrictive or structured intake food practices and that restrictive food parenting practices may be more harmful for children with OW/OB.

11:30

À Metabolic Processing In Taste Cells Contributes To The Hedonic Appeal Of Sugars (New Investigator Travel Awardee)

Aracely Simental-Ramos¹, Ahyun Jung¹, Sandrine Chometton³, Lindsey Schier^{1,2}

¹Neuroscience Graduate Program, University of Southern California, Los Angeles, CA, United States, ²Department of Biological Sciences, University of Southern California, Los Angeles, CA, United States, ³French National Institute for Agriculture, Food, and Environment, Dijon, France

Cephalic sensory and digestive processing of sugars directly affect downstream events like glucoregulation and satiation. We previously showed that dietary experience with simple sugars (SugExp), glucose and fructose (18 days, 0.316, 0.56, 1.1 M, 1 sugar/day), reinforces taste-driven responsivity to glucose, and this is mediated by a metabolic, glucokinase-linked, sensor in the taste cells. SugExp also boosts licking for maltose, a glucose disaccharide, especially in mice that lack a critical intermediary in sweet transduction, TRPM5. However, maltose does not directly engage with glucokinase in its bound form. Therefore, here we tested two related hypotheses. First, we assessed whether lingual glucokinase is required to express a relative preference for maltose in SugExp mice. Second, we tested whether lingual maltose glucoamylase (MGAM), a digestive enzyme that is expressed in taste bud cells that generates free glucose for nearby sweet receptors and glucosensors, contributes to the behavioral attraction to maltose. We found that knockdown of glucokinase in the major taste fields with a short hairpin RNA (shRNA) reversed the acquired preference for maltose in SugExp, sweet-sensitive and subsensitive mice. Finally, shRNA-mediated silencing of MGAM in the major taste fields significantly reduced licking avidity for 0.6 M maltose, as measured by lick burst size, in a short licking test, in naïve mice. Taken together, these results provide the first evidence that enzymatic and metabolic processing of certain sugars at the very first site of nutrient detection amplifies the hedonic impact of sugar, perhaps especially when sweet taste is deficient.

11:45

Weight Suppression Not Body Mass Influences Taste Liking

Sarah H Guo, Kimberly R Smith

Department of Psychiatry and Behavioral Science, Johns Hopkins School of Medicine, Baltimore, MD, United States

Taste liking plays a pivotal role in food choice and ingestive behaviors, yet the relationship between body mass and taste liking remains unclear in the literature. This study aimed to examine reported taste liking across individuals stratified by lean, overweight, and obese BMI groups. Sixty adults (53% women) rated their taste liking for 12 mixtures varying in added sugar (0%, 10%, or 20%) and milkfat (0%, 3.3%, 11%, or 37.5%) on visual analogue scales (VAS; -100=greatest disliking ever experienced, +100= greatest liking ever experienced). Analyses conducted on taste mixtures collapsed across fat or sugar concentration revealed no differences in liking ratings across BMI groups. Participants were then grouped into tertiles based on their degree of weight suppression (maximum lifetime body weight – current body weight), and analyses were conducted on the first (no weight suppression; NS) and third (22.9 ± 9.3 lbs weight suppression; WS) tertiles. Main effects of group and concentration were found for fat mixtures and sugar mixtures as well as a significant group by sugar concentration interaction. Taste liking ratings for fat concentration followed an inverted U-shaped curve in both groups, with the WS group reporting greater liking of 3.3% fat mixtures relative to the NS group. Taste mixtures with added sugar were liked more than mixtures without added sugar in both groups, with the WS group reporting greater liking of all sugar added mixtures relative to the 0% added sugar mixtures and relative to ratings in the NS group. The NS group gave similar neutral ratings for mixtures across sugar concentrations. These data indicate a role of weight suppression in taste liking and the importance of its consideration when investigating taste perception and reward.

12:00

Stomach Surgery Cuts Down Sugar Preference

Emily Alway^{1,2,3}, Alam Coss^{1,2}, Carlos Puerto Hernandez^{1,2}, Laila Khan-Farooqi^{1,2}, M. Maya Kaelberer^{1,2}, Diego V. Bohorquez^{1,2}

Bariatric surgery is currently the only effective and durable treatment for obesity and diabetes. While the health benefits of these gut surgeries are evident, the mechanisms of metabolic improvement remain unclear. However, patients have increased levels of circulating gut satiety hormones and decreased preference for sweet foods following surgery. Sugars are sensed by specialized intestinal cells known as neuropod cells. Neuropod cells rapidly signal the presence of intestinal sugar to the vagus nerve to drive sugar preference. We hypothesize that this neuropod cell to vagus nerve sugar signaling circuit results in decreased sugar preference after bariatric surgery. First, we used the IntelliCage, a social homecage, to offer mice three days of continuous and simultaneous choice of sugar, sweetener, protein, and fat to assess preference of high-fat diet-fed male mice before and after bariatric surgery. We found that sugar preference in sham-operated mice did not change after surgery, but sucrose preference in mice that received bariatric surgery decreased while preference for the artificial sweetener sucralose increased. With qPCR, we found surgery-specific changes in neuropod cell transcripts related to sugar signaling. We then imaged calcium transients in cultured vagal nodose neurons from sham and bariatric surgery mice. Neurons from bariatric surgery mice increased in sensitivity. These concordant shifts in sugar preference and physiology may reveal the neuropod cell as a key mediator of the improvements in metabolism after bariatric surgery. By investigating these critical interfaces between food environment and metabolism, we can identify pharmacological targets to alter the pathogenesis of diet-related illnesses such as obesity and diabetes.

12:15 - 1:45 PM	On Own
Lunch	

1:45 - 2:45 PM	Ballroom I-II
MARS Lecture 3	

Chair(s): Bobby Cheon

1:45

The Role Of Food Sensory Cues In Eating Behaviour, Food Intake And Health

Ciaran Forde

Wageningen University and Research, Wageningen, Netherlands

Food choice and energy intake are more strongly influenced by the sensory and cognitive aspects of eating than the underlying nutritive properties of the food being consumed, yet chronic disease and ill-health result from prolonged exposure to diets low in nutrients and high in energy-density. The role of dietary patterns in the development of related chronic conditions is undisputed, yet this knowledge is of little value if we cannot change these unhealthy food patterns. A foods sensory properties shape 'what', 'how much' and 'why' we eat, and influence the learning that drives our dietary patterns to influence health and well-being across the lifespan. Not all calories are equal, and food texture, taste and aroma direct food choice, inform our eating behaviours and through this can influence meal size. We have demonstrated the impact of consuming energy-dense foods at faster rates that sustain higher energy intakes across controlled feeding trials, in birth cohorts and population dietary intake studies. Our research on bolus properties and has highlighted the metabolic impact of eating behaviours on glucose-control, satiety, and microbiome metabolites. Food sensory properties are an under-utilized tool in promoting healthier eating behaviours, and we have shown food texture can be used to consistently moderate eating behaviour and the energy consumed within and across meals. Addressing the serious public health challenges posed by the food environment will require changes in dietary patterns and eating behaviours that are easy for consumers to adopt. Using a foods sensory properties makes it possible to promote healthier eating behaviour and can inform the development of successful dietary strategies that keep enjoyment and satisfaction at the heart of healthy eating.

2:45 - 3:30 PM	Riverwalk A
Coffee Break & Exhibits	

3:30 - 5:10 PM	Ballroom III
Symposium 5: Thirst & Salt Appetite	

Chair(s): Caitlin Baumer-Harrison

3:30

Isolating Thirst-Relevant Substrates From A System That Controls Thirst And Hunger: Focusing On Glucagon-Like Peptide-1

Derek Daniels

Department of Biological Sciences and the Center for Ingestive Behavior Research, University at Buffalo, SUNY, Buffalo, NY, United States

Numerous central signals play roles in the control of both eating and drinking. Studying these signals can be further complicated because changes in eating and affect drinking and changes in drinking can affect eating. The glucagon-like peptide-1 (GLP-1) system illustrates this complexity. GLP-1 receptor activation decreases eating and drinking and eating and drinking affect elements of the endogenous GLP-1 system, but with some observed differences. For instance, eating after food deprivation affects central and peripheral GLP-1, but drinking after water deprivation appears to affect only central GLP-1. This presentation will describe current work in the laboratory that is using the vasopressin deficient Brattleboro rat to identify other differences in the eating- and drinking-relevant substrates.

3:55

Water Intake, Hydration, And Weight Management: The Glass Is Half-Full!

Brenda M. Davy

Virginia Tech , Blacksburg, VA, United States

The lack of practical and effective strategies to manage hunger and adhere to a weight management intervention represents a critical barrier to the weight management field. In proof-of-of-concept efficacy studies, we demonstrated that premeal water consumption (500 ml) acutely reduced perceived hunger and meal energy intake among middle-aged and older adults, and that premeal water consumption (500 ml, 3 times per day) increased the amount of weight lost after 12 weeks among middle-aged and older adults with overweight or obesity. However, water consumption may be important for weight management regardless of when it is consumed. This presentation will address what is known about water intake, hydration status, and weight control. Potential mechanisms by which water consumption could impact appetite and hypocaloric diet adherence will be addressed.

4:20

Role Of Brain Angiotensin Ii In Salt Palatability

Laurival A. De Luca Jr.

UNESP, Araraquara, SP, Brazil

The "hedonic shift" of salty taste - aversive to hedonic according to physiological status (from euhydration to sodium

depletion) - corresponds to an increase in salt palatability. This is supported by taste reactivity tests in which we count standardized orofacial motor responses - “hedonic” or “aversive” - to a small intraoral infusion of hypertonic NaCl. Brain angiotensin II has a established role in facilitating sodium appetite, i.e., hypertonic NaCl intake by sodium-depleted rats. Experiments from our group suggest that this role also subserves the hedonic shift (Zenatti et al., 2021; Fernandes et al., 2022). We saw that, firstly, brain antagonism of angiotensin II AT1 receptors produces a substantial increase in aversive orofacial motor responses to 0.3 M NaCl. Moreover, systemic injection of a converting enzyme blocker, at a dose that crosses the blood-brain barrier, reduced by more than 50% hedonic responses when it inhibited 0.3 M NaCl intake in a sodium intake test. Second, episodic production of rapid onset sodium appetite by treating rats with natriuretic furosemide combined with low dose of captopril (“Furo/Cap”) - to enhance early increase in brain production of angiotensin II - increased hedonic responses and reduced aversive responses to 0.3 M NaCl. Furo/Cap did not alter orofacial responses to an intraoral infusion of capsaicin that preceded each salt infusion; this suggests that the angiotensin II-mediated hedonic shift is independent from reduction in oral nociception typically generated by hypertonic salt. In addition to the known role of angiotensin II in motivating the search for sodium intake, this peptide might also play an essential role in the affective or emotional component of salty taste.

4:45

Evaluating The Role Of Brain Angiotensin Signaling In Thirst And Salt Appetite

Joel Geerling

Oral Session 7: What did I just eat? Ultra-processed Foods and Macronutrients

Chair(s): Alex DiFeleciontonio

3:30

Ultra-Processed Food Consumption And Weight Gain: A Meta-Analysis Of Prospective Studies And An Examination Of Likelihood That Unmeasured Confounding Could Explain Away Findings

Eric Robinson, Andrew Jones

University Of Liverpool, Liverpool, United Kingdom

Higher consumption of ultra-processed foods (UPF) has been associated with a range of negative health outcomes, including risk of weight gain and development of obesity. Most observational studies on body weight have been cross-sectional and no meta-analyses focus on prospective studies. We systematically identified and meta-analysed prospective studies on UPF consumption and weight gain in adults (N=6). Studies defined UPF dietary share through the Nova classification system and by examining % of daily energy intake from the UPF category. Meta-analysis indicated that participants with the highest consumption of UPFs in the diet (quartile 4) were at 28% increased risk of weight gain [HR = 1.28, 95%CI = 1.18, 1.39], vs. those with the lowest consumption (quartile 1). Next, we used the E-value method to assess whether unmeasured confounding variables (i.e. not controlled for in any of the meta-analysed studies) could plausibly explain why UPF consumption is associated with weight gain prospectively. A minimum E = 1.65-1.89 indicated that an unaccounted for variable with a small-moderate sized association with both UPF consumption and weight gain could fully attenuate the UPF-weight gain effect observed. We next use data from a range of systematic reviews and meta-analyses to model if mental health symptoms, food insecurity and/or trait problematic eating tendencies could independently or collectively contribute to E = 1.65-1.89. Analysis was suggestive that they could do and are therefore potential confounders of importance that have not been accounted for in studies to date. Diets high in UPFs are prospectively associated with increased risk of weight gain. It is at least feasible that unmeasured confounding could attenuate some or all of this association.

3:45

Consistent Effects Of Food Texture Of Ultra-Processed Foods On Eating Rate And Energy Intake Across Meals, Days, And DietsMarlou Lasschuijt¹, Lise Heuven^{1,2}, Marieke van Bruinessen¹, Els Siebelink¹, Markus Stieger^{1,2}, Kees de Graaf¹, Ciarán Forde¹¹Division of Human Nutrition and health, Wageningen University, Wageningen, Netherlands, ²Food Quality and Design group, Wageningen University, Wageningen, Netherlands

Chronic food overconsumption and consequent body weight gain can lead to obesity and non-communicable diseases. Sensory and nutritional properties of food affect food consumption. Examples of such properties are food texture and energy density, that combined determine energy intake rate (EIR, kcals/min), with faster EIR leading to higher energy intakes. The extent to which EIR can be manipulated to moderate energy intake from ultra-processed foods (UPF) is unknown. Therefore, the objective was to determine the effect of texture and energy density on energy intake at the level of the meal, day and diet. To study this, three within-subject *ad libitum* feeding studies were performed, all including healthy participants (meal level N=69, day level N=18, diet level N=20). In the meal-level study participants consumed UPF meals that varied in texture based eating rates (ER) and energy density (ED). Within the day-level study participants consumed menus that differed in processing level and ER (Slow, Fast). Within the diet study, participants were provided a 12-day diet of UPF-fast or UPF-slow meals for breakfast and dinner. Within a meal, energy intake was 50% lower for the slow-low ED meals compared to fast-high ED meals (573±45kcal, P<.001). At the level of the day, hard texture led to a slower ER which led to a 33% (571±135 kcal) reduction in energy intake compared to the soft texture conditions. These findings were confirmed at the diet-level, where participants' food intake was (7%) lower in the slow ER arm compared to the fast ER arm. These findings show that meal texture can moderate *ad libitum* energy intake from ultra-processed foods, this highlights opportunities to manipulate food texture and ED when reformulating foods to reduce their risk of energy overconsumption.

4:00

Sucrose Overconsumption Impairs AgRP Neuron Dynamics And Promotes Fructose IntakeCarolyn M Lorch^{1,2}, Nikolas W Hayes^{1,3}, Jessica L Xia¹, Stefan W Fleps^{1,4}, Hayley E McMorow^{1,3}, Haley S Province^{1,3}, Joshua A Frydman¹, Jones G Parker⁴, Lisa R Beutler¹¹Department of Medicine, Northwestern University, Chicago, IL, United States, ²Driskill Graduate Program in Life Sciences, Northwestern University, Chicago, IL, United States, ³Northwestern University Interdepartmental Neuroscience, Northwestern University, Chicago, IL, United States, ⁴Department of Neuroscience, Northwestern University, Chicago, IL, United States

Rapid gut-brain communication is critical to maintain energy balance and is disrupted in diet-induced obesity through mechanisms that remain incompletely understood. Specifically, the role of carbohydrate overconsumption in the regulation of interoceptive circuits has been minimally examined *in vivo*. We recently reported that an obesogenic high-sucrose diet (HSD) selectively blunts post-ingestive silencing of hunger-promoting AgRP neurons in response to glucose, while not impacting AgRP neuron responses to fructose. Here, we report preliminary findings that intake of glucose-containing food pellets is diminished following a HSD, while HSD-fed mice retain a consistent appetite for fructose-containing pellets. Ongoing work is aimed at determining whether reduced glucose preference is the direct result of its blunted ability to inhibit AgRP neurons. Taken together, our findings reveal that sugar overconsumption differentially alters neural responses to, preference for, and intake of individual monosaccharides in a manner that favors fructose intake.

4:15

Effects Of Food Processing On Inflammation In The BrainLillian Brouwer¹, Zach Hutelin², Bert Herald², Mary Elizabeth Baugh², Monica Ahrens³, Alexandra Hanlon³, Susan Melhorn⁴, Alexandra DiFeleciontonio⁵¹Virginia Tech Carilion School of Medicine, Roanoke, VA, United States, ²Fralin Biomedical Research Institute, Roanoke,

VA, United States, ³Center for Biostatistics and Health Data Science, Virginia Tech, Roanoke, VA, United States,

⁴University of Washington, Department of Medicine, Seattle, WA, United States, ⁵Department of Human Nutrition, Foods, and Exercise, Virginia Tech, Blacksburg, VA, United States

Ultra-processed foods (UPF) make up 58% of calories consumed in the US. While it is known that ingredients in UPF produce inflammation in the gastrointestinal system and disrupt the gut microbiome, little is known about UPF's impact on inflammation in the brain. Brain inflammation and insulin resistance have been implicated in cognitive deficits, and reduced insulin signaling in the brain affects dopamine metabolism and release. The mediobasal hypothalamus (MBH) controls energy homeostasis, and hypothalamic inflammation precedes the onset of diet-induced obesity in rodents and predicts adiposity gain in young children. In this prospective study (target n=52), habitual food consumption was measured via 24-hour dietary recall surveys. A fast spin-echo T2 weighted image collected via magnetic resonance imaging was used to determine the degree of MBH brain gliosis as a measure of brain inflammation. T2-weighted images have no absolute scale, so a T2 signal ratio (MBH/amygdala (AMY)) was used to compare MBH signal intensity between individuals. Greater signal ratios indicate higher T2 signal intensity and are consistent with the presence of inflammation and gliosis in the MBH. Thus far, we have evaluated hypothalamic gliosis in 10 subjects, with recruitment ongoing. We observed a relationship between MBH/AMY and % calories from UPF ($r=.32$, $p=.37$), protein ($r=.19$, $p=.61$) and grams of fiber ($r=.37$, $p=.29$), but not % calories from fat ($r=-.09$, $p=.80$) and carbs ($r=-.03$, $p=.94$). This is an ongoing study to understand how UPFs impact inflammation in the brain.

4:30

High Energy Diet Effects On The Mediobasal Hypothalamus: Inflammation, Astrocytes And Obesity.

Anais Bouchat, Luca Papini, Christelle Le Foll

Institute of Veterinary Physiology, University of Zurich, Zurich, Switzerland

Long-term high-energy diet (HED) feeding results in an obese phenotype. Although not entirely elucidated yet, it is also accompanied by inflammation and gliosis in the mediobasal hypothalamus (MBH). Diet-induced obese (DIO) rats have defective nutrient sensing before becoming obese. We hypothesize that MBH glial inflammation in DIO rats plays a major role in the development and maintenance of the obese phenotype. We first found that standard diet (SD)-fed DIO adult male rats displayed a heightened astrocyte density in the MBH as compared to diet-resistant (DR) rats. MBH astrocyte density was decreased in DIO rats following 4 weeks of HED, while it remained unchanged in DR rats. However, after 10 weeks on HED, MBH mRNA levels of gliosis-, inflammatory- and food intake-related genes were increased in HED-fed DIO rats as compared to HED-fed DR rats. Unexpectedly, these results did not correlate with GFAP nor Iba1 immunostaining, showing no significant increase in gliosis markers. In an ongoing study, we now aim at evaluating MBH cytokines protein levels following exposure to HED for different durations. Next, to test our hypothesis, we depleted a key inflammatory protein, IKKB, in MBH astrocytes of DR and DIO rats using an AAV-GFAP IKKB viral approach. When IKKB was depleted from MBH astrocytes in 4-week-old rats prior to HED exposure, it mitigated the development of the obese phenotype in DIO rats. We then assessed whether the obese phenotype can be reversed once installed. After being exposed to HED for 4 weeks, DR and DIO rats received either a control or an IKKB-GFAP AAV and were kept on HED for 5 more weeks. IKKB depletion failed to improve any obesity markers suggesting that once the obese phenotype is installed, it cannot be overcome by reducing MBH inflammation.

4:45

Resting-State Connectivity Between The Salience Network And Left Thalamus In Adolescents Predicts Sugar-Sweetened Beverage Intake A Year Later.

Grace E Shearrer^{1,2,3}, Muzayyana Akhmadjonova^{1,2}

¹Graduate Program in Neuroscience, University of Wyoming, Laramie, WY, United States, ²Department of Family and Consumer Sciences, University of Wyoming, Laramie, WY, United States, ³School of Computing, University of Wyoming, Laramie, WY, United States

Sugar sweetened beverage (SSB) consumption is associated with increased adiposity in childhood. We aimed to predict SSB intake at year-2 from year-1 resting-state functional magnetic resonance (rsfMRI) connectivity in children. We used baseline demographic and rsfMRI data and year-2 SSB intake data (Block Kids Food Survey) from the Adolescent Brain Cognitive Development study. Participants were included if they had complete baseline rsfMRI correlation data (subcortical 19 regions of interest [ROI] to Gordon cortical 12-network ROIs and cortical to cortical), height and weight, household income, sex, age; and year-2 SSB intake data. We defined SSB intake groups as low (<8 foz/day) and high (>16 foz/day). Groups were matched on sex, age, body mass index percentile (BMI%) and household income using nearest neighbor (n/SSBgroup=1854, age=9.95±0.63, BMI%=63.1±0.02, sexF=1467). We used a grid search linear support vector classifier ($n_{\text{train}}=2085$, $n_{\text{test}}=927$) with univariate feature selection to determine how many and which ROIs to include in our model out of 416 baseline ROIs. Selected features were used in a binary logistic regression (bootstrapping=1000) to predict high SSB intake at year-two ($n_{\text{train}}=741$, $n_{\text{test}}=186$). All training and testing groups were exclusive. All modeling was performed in Python using SciKit Learn. Stronger connectivity between the salience network and left thalamus (OR=0.57, CI=-1.65:0, $p=0.05$) was related to lower odds of high SSB consumption at year-2. Previous research shows connectivity between the salience network (insula, anterior cingulate, and ventral striatum) and the thalamus is related to balancing homeostatic demands. Our work suggests that weakening this homeostatic connectivity predisposes children to higher SSB intake.

5:00

Energy-To-Satiety Ratio Explains The Effect Of Combining Fat And Carbohydrate On Food Reward

Annika N. Flynn, Peter J. Rogers, Jeffrey M. Brunstrom

Nutrition and Behaviour Unit, School of Psychological Science, University of Bristol, Bristol, United Kingdom

Combining fat and carbohydrate (carb) increases food reward. Previously, we hypothesised that the underlying mechanism is *reduced* satiety – foods comprising a more equal ratio of carb and fat deliver *less* satiety per calorie (i.e., have a higher energy-to-satiety ratio). In turn, these foods are more rewarding because they facilitate energy intake – the goal of eating is to ingest nutrients, not to achieve satiety. To test this, we conducted a study in the US ($N=148$ participants, 36 foods) and a study in the UK ($N=150$ participants, 24 foods). In both cases, participants evaluated high carb (C), high fat (F), and 'combo' (equal fat/carb) foods. As anticipated, in both studies, the combo foods were (1) rated more liked (taste pleasantness means (SD): UK C= 51.9 (13.1), F= 52.9 (15.8), combo= 66.6 (12.8), $p<.001$; US C= 59.5 (16.0), F= 58.4 (18.3), combo=

64.1 (14.2), $p < .001$), (2) rated more rewarding (desire to eat means (SD): UK C=37.4 (15.8), F= 38.5 (18.0), combo= 51.9 (17.9), $p < .001$; US C= 46.8 (19.1), F= 47.0 (21.7), combo= 53.3 (18.0), $p < .001$) and (3) perceived less satiating (comfortably full (kcal) means (SD): UK C= 271.9 (162.7), F= 301.8 (168.0), combo= 344.2 (164.0), $p < .001$; US C= 201.5 (74.3), F= 200.6 (75.7), combo= 228.2 (74.4), $p < .001$). The results for other measures (ideal portion (kcal), maximum portion (kcal) and rated sickliness) were also fully consistent with our hypothesis (all $p < .001$). Together, these findings provide strong support for our interpretation of the greater reward value (via greater liking) of combo foods in terms of energy-to-satiety ratio. More generally, they highlight a form of nutritional intelligence, whereby a function of food reward is to motivate the consumption of foods that maximise nutrient intake.

Saturday, July 13, 2024

8:00 - 4:15 PM	Sheraton Promenade West
Registration	
8:30 - 10:10 AM	Ballroom III
Symposium 6: Nutritional Bases of Food Reward	

Chair(s): Christopher Morrison

8:30

Lack Of Brain Dopamine Response To An Ultra-Processed Milkshake High In Fat And Sugar In Humans

Valerie Darcey^{1,2}, Juen Guo¹, Stephanie Chung^{3,4}, Amber Courville⁴, Isabelle Gallagher¹, Peter Herscovitch⁵, Rebecca Howard¹, Melissa LaNoire¹, Lauren Milley¹, Alex Schick¹, Michael Stagliano³, Sara Turner⁶, Shanna Yang⁶, Nan Zhai¹, Megan Zhou¹, Kevin Hall¹

¹Integrative Physiology Section, National Institute of Diabetes & Digestive & Kidney Diseases, Bethesda, MD, United States, ²Center on Compulsive Behaviors, Intramural Research Program, National Institutes of Health, Bethesda, MD, United States, ³Section on Pediatric Diabetes Metabolism and Obesity, National Institute of Diabetes & Digestive & Kidney Diseases, Bethesda, MD, United States, ⁴Human Energy and Body Weight Regulation Core, National Institute of Diabetes & Digestive & Kidney Diseases, Bethesda, MD, United States, ⁵Clinical Center Positron Emission Tomography Department, National Institutes of Health, Bethesda, MD, United States, ⁶Clinical Center Nutrition Department, National Institutes of Health, Bethesda, MD, United States

Ultra-processed foods (UPF) high in fat and sugar have been likened to drugs of abuse in that they are believed to reliably elicit a large dopamine (DA) response in brain reward regions. Preclinically, palatable food intake elevates DA and obesity may blunt this effect. Gastric infusions suggest that post-oral, gut-brain signaling elicit prolonged striatal DA responses, though, these concepts have not been fully tested in humans. We measured DA responses to a high-fat/sugar UPF milkshake as a part of an inpatient feeding study using PET (n=50 [33F]; 31.9±7.2 years old; 54% African Amer.; BMIs 20.3 - 44.8 kg/m²). Subjects ate the provided eucaloric diet (30% fat, 50% carb.) for 6.8±1.1 days before an overnight-fasted [11C]raclopride scan, followed by a 2nd [11C]raclopride scan 30 min. after drinking an 8 oz UPF shake (418 kcal; 60% fat, 33% carb.). Reduced binding potential (D2BP) (shake vs. fasting) was reflective of a DA “response”. Contrary to expectations, no significant striatal DA response after the UPF milkshake was observed (fasting D2BP 2.90 (0.06SE); milkshake D2BP 2.91 (0.06SE), p=0.616). DA response tended to be weakly linked to BMI (r=-0.276, p=0.052). In exploratory tests, “Responders” (n=29; D2BP %Δ -4.3(0.7SE)) both liked (p=0.036) and wanted more milkshake (p=0.003) vs those without a DA response (n=21; D2BP %Δ 8.5(2.0SE)). In “Responders”, striatal milkshake DA response increased with fasting hunger (r= 0.45, p=0.024). Surprisingly, consuming an UPF milkshake did not result in significant striatal DA responses in a large sample spanning a wide BMI range. Individual variation in perception of hedonic and appetitive state warrant investigation as mechanisms by which UPFs result in excess energy intake.

8:55

Sugar Reward Recruits Multiple Molecular Signaling Pathways In The Taste System

Lindsey A. Schier

University of Southern California, Los Angeles, CA, United States

Taste is a primary determinant of food palatability, and, in turn, dietary choice. Although we come wired to detect and respond to key classes of biologically-significant chemicals in our food environment, the hedonic appeal of foods can be revised with ingestive experience. This can involve learning about other cues associated with the food (e.g., odors), but whether it also involves lasting changes to the taste inputs themselves has been largely unexplored. We found that dietary exposure to metabolically-distinct sugars, glucose and fructose, conditions a strong preference for the taste of glucose over that of fructose. Since both sugars activate a common sweet taste receptor, we hypothesized that one or both sugars can engage an alternative receptor, whose signal becomes more rewarding with experience. In a series of studies, we uncovered a metabolic sensor, involving glucokinase, expressed in taste cells, which is not only involved in the unconditioned detection of glucose, but is upregulated with sugar experience, and is required to express the conditioned preference for glucose (and other glucose-yielding sugars) in sweet-sensitive mice. Interestingly, sweet-blind mice appear to also rely on a metabolism-independent glucosensor, involving sodium-linked electrogenic glucose transport in taste cells, to reinforce glucose intake. The collective results reveal several previously unrecognized features of sugar reward, namely the taste system has multiple mechanisms for detecting and discriminating glucose from other sweeteners, dietary factors influence the expression of these peripheral signaling systems to affect sensitivity, and the brain can take advantage of these taste cues to bias intake towards energetically-advantageous substrates.

9:20

Examining The Role Of Objective And Perceived Nutritional Characteristics Of Foods As Predictors Of Liking And Control Over Eating In The Satmap Project. (Supported By The Ssib International Foundational Fund Given In Memory Of Drs. Jacques Le Magnen (France), Anton Steffens (The Netherlands), Jacob Steiner (Israel), Steven Cooper (The United Kingdom))

Graham Finlayson¹, Clarissa Dakin¹, Angelika Baaij², Nicola Buckland³, Michelle Dalton⁴, James R. Stubbs¹

The value people assign to foods is determined by their intrinsic properties (nutritional, sensory) and moderated by individual factors such as traits, states and beliefs. There is a need for more systematic, structured analyses of the characteristics that explain our cognitions about food such as liking and perceived control over eating. Across three sequential survey designs, ~500 foods were sampled and photographed from databases containing nutritional composition data of >70,000 ready-to-eat UK foods. Each image was evaluated by sub-samples of 70-500 participants from the UK (N=3,296). Mean ratings for perceived nutritional, sensory and cognitive characteristics of the foods were calculated. In this study, the primary outcomes of interest were food pleasantness (liking) and control over eating (hedonic overeating). Spearman's Rho was used to correlate individual food-level characteristics with liking and hedonic overeating. Linear mixed models tested combinations of nutritional characteristics as predictors of liking and hedonic overeating. These ongoing analyses permit tests of hypotheses relating protein, sugar, energy density, carbohydrate:fat ratio and degree of processing to food reward, within and between samples. Associations between liking, hedonic overeating, and beliefs about food functionality (healthiness, satiating capacity, potential for weight management) were also examined. Future work will explore the extent to which individual factors moderate relationships between food characteristics and food reward. The approaches developed in this research could produce a reference system to support reformulation of foods and improve dietary management of weight and health.

9:45

Nutrients And Sensory Food Qualities Guide Value-Based Economic Choices And Reinforcement Learning In Monkeys (Supported By The Ssib International Foundational Fund Given In Memory Of Drs. Jacques Le Magnen (France), Anton Steffens (The Netherlands), Jacob Steiner (Israel), Steven Cooper (The United Kingdom))

Fabian Grabenhorst

University of Oxford, Oxford, United Kingdom

Value is a foundational concept in reinforcement learning and economic choice theory. In these frameworks, individuals choose by assigning values to objects and learn by updating values with experience. We investigate how such values derive from the biologically critical components of foods: their nutrients and sensory qualities. I will review recent findings from behavioral experiments and single-neuron recordings in macaques showing that (i) nutrients and sensory food qualities influence human-like economic food preferences (Huang, Sutcliffe and Grabenhorst, 2021, PNAS); (ii) nutrients guide reinforcement learning (Huang and Grabenhorst, 2023, JNeurosci); (iii) amygdala neurons encode nutrients, sensory food components, and their integration to subjective values. Specifically, when monkeys choose nutrient-defined liquids of varying amounts, they consistently prefer fat and sugar to low-nutrient alternatives. Rather than maximizing energy, they assign value to specific nutrients, flexibly trading them for reward amounts. Psychophysical nutrient-value functions accurately model these preferences to explain individual differences and nutrient-sensitive reinforcement learning. To identify the sensory basis of nutrient values, we developed engineering tools that measure food textures on biological surfaces (pig tongues), mimicking oral conditions. Subjective valuations of food textures (viscosity, sliding friction) mediated monkeys' fat preferences, suggesting a texture-sensing mechanism for nutrient valuation. Our findings identify nutrients and food textures as critical rewards that guide economic choices and reinforcement learning. Our approach holds promise for studying neural food-reward mechanisms in primates to better understand eating behavior and obesity.

Oral Session 8: Not Another Bite: Satiety, Satiety

Chair(s): Barbara Rolls

8:30

Examining The Role Of Nutritional, Sensory And Perceptual Characteristics In Perceived Satiety Of 312 Commonly Consumed Foods In The Uk Diet. (New Investigator Travel Awardee)

Clarissa A Dakin, Graham Finlayson, R. James Stubbs

Appetite Control and Energy Balance Research Group (ACEB), School of Psychology, Faculty of Medicine and Health, Leeds, United Kingdom

Introduction: Understanding the satiety value of foods is critical for obesity prevention and management. However, modelling satiety is complex because it requires integration of nutritional (e.g. macronutrients), sensory (e.g. bitterness) and perceptual/cognitive (e.g. pleasantness) characteristics of foods. The aim of the study was to explore the degree to which nutritional, sensory, and perceptual/cognitive characteristics of common foods predict perceived satiety (PS). **Methods:** A representative sample of UK adults including 2,010 participants (51% female, mean age = 45 years, mean BMI =

26.98kg/m²), rated PS and 20 nutritional, sensory and perceptual/cognitive characteristics of 10 randomly selected standardised portions (240kcal) of 10 common foods chosen from a larger (n = 312) representative sample of UK foods. Linear mixed models examined nutritional, sensory and perceptual/cognitive characteristics as predictors of PS. **Results:** Sugar (g), salt (g), and kcal (g) were negative predictors of PS, whilst protein (%) and carbohydrates (%) were positive predictors of PS (p < .001). Adding sensory and perceptual/cognitive characteristics increased the variance explained in PS and an ANOVA found that the more complex model provided a better fit for the data (p < .001). **Conclusions:** Overall, PS is a complex construct that is not fully explained by simple nutritional models. Integrated models that account for nutritional, sensory, and perceptual/cognitive characteristics offer a more comprehensive account. The findings have the potential to improve scientific understanding of the satiety value of foods. If the resulting models are robust, then novel foods or diet plans could be designed that maximise PS and support management of weight and health.

8:45

Passive Overconsumption? Limited Evidence Of Compensation In Meal Size When Consuming Foods High In Energy Density: Two Randomised Crossover ExperimentsAmy H Finlay¹, Emma Boyland¹, Andrew Jones², Tess Langfield¹, Eve Bending¹, Manraj S Malhi¹, Eric Robinson¹¹University of Liverpool, Liverpool, United Kingdom, ²Liverpool John Moores, Liverpool, United Kingdom

Research has drawn contradictory conclusions as to whether humans adjust meal size based on meal energy density (ED) or exhibit 'passive overconsumption'. Recent observational research suggests that meal EDs greater than 1.7-2kcal/g are compensated for through consumption of smaller meal sizes. We tested the relationship between ED and meal size by examining consumption at low (~1.0kcal/g), medium (1.7-2.0kcal/g) and high (>3.0kcal/g) EDs. In the first of two randomised crossover experiments, n=34 adult participants were served a lunch including a familiar low, medium or high ED dessert to eat ad libitum. In experiment 2, n=32 adult participants were served a lunch covertly manipulated to be low, medium or high ED to eat ad libitum. In experiment 2, later energy intake in the day was also measured. In experiment 1, participants consumed a similar amount of energy in low and medium ED conditions. The high ED food was associated with an increased intake of approximately 240kcal compared to medium (p<.001, Cohen's d=2.31) and low (p<.001, Cohen's d=4.42) ED foods. In experiment 2, there were no significant differences in meal size between ED conditions, resulting in a largely linear relationship between meal ED and energy intake ('passive overconsumption'). There were no differences in later energy intake between ED conditions. Contrary to recent suggestions, foods higher in ED were not associated with adjustments to meal size and were associated with increased energy intake. Reformulation of high ED foods may be an effective population level approach to reducing energy intake and obesity.

9:00

Brainstem Neuropeptide Neurons Regulating Satiety

Srikanta Chowdhury, Alexander R. Nectow

Columbia University, New York, NY, United States

Hunger is a fundamental drive, evolutionarily hard-wired to ensure that an animal has sufficient energy to survive and reproduce. Just as important as knowing when to eat is for an animal to know when not to eat. Here, using spatially-resolved, single cell translational phenotyping, we characterize a small population of neuropeptidergic neurons in the brainstem's dorsal raphe nucleus (DRN) and describe how they regulate satiety. These neurons track food from sensory presentation through ingestion and consequently drive a short-lived, yet hysteretic meal termination signal with a built-in delay. They are also well-poised to sense and respond to ingestion, expressing a host of metabolic signaling factors and receiving multi-synaptic input from sensory loci and the gut. Together, this work demonstrates how a small brainstem cell type regulates satiety and identifies a likely conserved cellular mechanism that transforms diverse neurohumoral signals into a key behavioral output.

9:15

Brainstem Preproglucagon (Ppg) Neurons Modulate Physiological Satiety And Their Once Daily Activation Produces Sustained Weight Loss In Obese But Not Lean MiceWanqing Jiang¹, Cecilia Skoug¹, Marie Holt³, Imogen Hayter¹, Fiona M Gribble², Frank Reimann², Daniel I. Brierley¹, Stefan Trapp¹¹Centre for Cardiovascular and Metabolic Neuroscience, Department of Neuroscience, Physiology & Pharmacology, UCL, London, United Kingdom, ²Wellcome Trust/MRC Institute of Metabolic Science (IMS), Addenbrookes Hospital, University of Cambridge, Cambridge, United Kingdom, ³School of Life Sciences, University of Warwick, Coventry, United Kingdom

Glucagon-like peptide-1 (GLP-1) serves as both an incretin and anorexigenic neuropeptide. Neuronal GLP-1 is mainly released by preproglucagon (PPG) neurons in the nucleus tractus solitarius (NTS) and intermediate reticular nucleus (IRT) of the brainstem. Recent studies showed that GLP-1 receptor agonists suppress appetite independently of NTS PPG neurons,

and that activating these neurons potentiates the anorexigenic effects of GLP-1 receptor agonists, suggesting NTS PPG neurons to be a novel anti-obesity therapy target. However, the potential contribution of IRT PPG neurons to this therapeutic potential is unknown. We therefore assessed the anatomy and anti-obesity potential of these two PPG neuron populations. Despite proximity between NTS PPG neuron axon terminals and IRT PPG cell bodies, optogenetic activation of NTS PPG neurons did not elicit c-fos expression in IRT PPG neurons. Besides, both NTS and IRT PPG neurons project to similar areas, suggesting potential additive effects upon their activation. Next, we assessed the effect of viral ablation or chronic chemogenetic activation of both NTS and IRT PPG neurons together. Compared to controls, PPG-ablated mice showed significantly higher body weight six months post-surgery and increased *ad libitum* feeding, driven by elevated meal size and duration. Chemogenetic activation of PPG neurons significantly reduced food intake on the first day in lean mice, with the effect diminishing over 14-day repeated activation and no significant weight change. Conversely, in obese mice, repeated activation of PPG neurons over 14 days led to sustained significantly lower food intake and body weight. In conclusion, NTS and IRT PPG neurons regulate satiation under *ad libitum* feeding and are potential targets for anti-obesity therapy.

9:30

Satiety Insecurity May Mediate The Relationship Between Food Insecurity And Selection Of Larger Portion Sizes

Bobby K. Cheon¹, Matt B. Sirotty¹, Julia M. P. Bittner¹, Li Ling Lee², Aimee E. Pink^{3,4}

¹Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD, United States,

²Nanyang Business School, Nanyang Technological University, Singapore, Singapore, ³Institute of High Performance Computing (IHPC), Agency for Science, Technology and Research (A*STAR), Singapore, Singapore, ⁴Singapore Institute for Clinical Sciences (SICS), Agency for Science, Technology and Research (A*STAR), Singapore, Singapore

Food insecurity (FI) is associated with food responsiveness, overeating, and obesity, yet it is unclear how these appetitive motivations emerge from FI. One possibility is that experience of FI promotes enduring insecurities about maintaining fullness, which may motivate opportunistic consumption of larger portions and interfere with the ability to compensate for larger meals. We tested this by developing a novel measure of satiety insecurity, representing *subjective* concerns about maintaining sufficient fullness, in contrast to concerns about *actual* food access typically assessed by conventional FI measures. Across six studies (total N=1134) in the USA, UK, and Singapore, we tested whether satiety insecurity predicts selection of virtual portion sizes. Internal meta-analyses of these studies showed an overall indirect effect of satiety insecurity ($B=.05$, 95%CI: .02, .08) on the relationship between FI and portion size, such that greater FI was associated with higher satiety insecurity, which was associated with selection of larger virtual portion sizes across diverse foods. A laboratory experiment (N=55) revealed that higher satiety insecurity was also associated with selection of larger intended virtual dinner portion sizes when presented with a large hypothetical lunch portion ($b= 61.91$, 95%CI: 9.58, 114.24), but not associated with selected virtual dinner portion sizes when presented with a small hypothetical lunch portion. These results suggest satiety insecurity may be a mechanism for FI to contribute to excess energy intake, possibly by motivating selection and inhibiting compensation of larger portions.

9:45

Oral Xylitol Reduces Subsequent Total Energy Intake In Healthy Humans: A Randomized, Controlled, Crossover Trial

Emilie Flad^{1,2}, Anita Altstaedt^{1,2}, Christoph Beglinger^{1,2}, Lukas Van Oudenhove³, Bettina Woelnerhanssen^{1,2}, Anne Christin Meyer-Gerspach^{1,2}

¹St. Clara Research Ltd, Basel, Switzerland, ²University of Basel, Basel, Switzerland, ³Katholieke Universiteit Leuven, Leuven, Belgium

INTRODUCTION High daily sugar intake is associated with an increased risk of developing obesity and type 2 diabetes mellitus. Artificial low-caloric sweetener as sugar alternatives, such as acesulfame potassium (ace-K), might lead to overeating due to their lack of nutritive value. Therefore, the aim of this study was to investigate the effect of the low-caloric bulk sweetener xylitol on subsequent energy intake during an *ad libitum* test meal. **METHODS** In this randomized, controlled, crossover study, 20 healthy participants with normal BMI were included. During four study visits, participants received oral preloads containing either 33.5 g xylitol, 33.5 g sucrose, 167.5 mg ace-K dissolved in 300 mL water or 300 mL water as control. Fifteen minutes after the preload, participants were served an *ad libitum* test meal for 20 minutes. Total energy intake was assessed and ratings of appetite-related sensations (hunger, prospective food consumption, satiety, fullness) and blood samples (glucose, insulin) were collected at fixed time points. **RESULTS** The results show that i) total energy intake was significantly lower for xylitol and ace-K compared to sucrose, with no differences between xylitol and ace-K or water; ii) before the start of the test meal, appetite-related sensations did not differ between the four preloads; iii) plasma glucose did not increase after xylitol compared to sucrose with no differences between xylitol and ace-K or water; iv) plasma insulin was significantly lower after xylitol compared to sucrose but higher after xylitol compared to ace-K or water. **CONCLUSION** Orally administered xylitol prior to an *ad libitum* test meal reduces total energy intake compared to sucrose and leads to a lower increase in plasma glucose and insulin concentrations.

10:00

Increasing The Spiciness Of A Lunch Meal Slows Eating Rate And Reduces Energy Intake

Paige M. Cunningham, John E. Hayes

The Pennsylvania State University, University Park, PA, United States

Recent evidence suggests increasing oral burn by adding ground chilies to food can modify oral processing behaviors like eating rate, which may potentially affect intake. However, empirical data on the effect of oral burn on intake at an *ad libitum* meal is lacking. Here, we conducted a randomized crossover study ($n = 52$) to test how the addition of chiles to a lunch meal influenced (a) eating rate and (b) food intake. One week apart, adults (29% men) were video recorded while eating a lunch consisting of 650 g of beef chili (1.1 kcal/g) served with 450 g of water. A constant weight of paprika (hot: 100% hot paprika versus mild: a blend of 25% hot & 75% sweet paprika) was added to each to adjust burn. Meal duration was extracted from videos to calculate eating rate (g/min). Participants rated liking and spiciness on a VAS before and after consumption. Participants consumed 12% less (51 ± 19 kcal) of the hot chili compared to the mild chili ($p=0.009$), but consumed a similar amount of water ($p=0.23$). While initial ratings of burn were higher for the hot chili ($p<0.0001$), liking did not differ systematically ($p=0.88$), suggesting differences in intake were related to burn, not initial liking. Burn also influenced eating rate ($p=0.02$); the hot chili was consumed 12% slower (6.5 g/min) than the mild chili. When accounting for the effect of eating rate on intake ($p<0.0001$), the effect of burn was no longer significant ($p=0.13$), suggesting intake differences were

driven by eating rate. Overall, these findings reveal a mechanism by which increasing meal spiciness affects ad lib intake via oral processing, suggesting adding chilies to meals may help manage risk of overconsumption and obesity by reducing energy intake.

10:15 - 11:00 AM	Riverwalk A
Coffee Break & Exhibits	

11:00 - 12:00 PM	Ballroom I-II
MARS Lecture 4	

Chair(s): Faris M. Zuraikat

11:00

“The Big Three”: Properties Of Food That Drive Intake

Barbara J. Rolls

The Pennsylvania State University, University Park, PA, United States

Much of the interest in studying human eating behavior stems from a desire to characterize properties of foods that promote consumption and those that enhance satiety, with the goal of leveraging these influential properties to moderate energy intake. Macronutrient composition has been the focus of much of this research and advice on how to manage intake. Lately, the attention has been shared with ultraprocessing and hyperpalatability of foods based on claims that these factors drive overconsumption. Consistent effects of these properties on intake, however, are yet to be established along with the underlying mechanisms. While we continue to build new ideas about aspects of foods that influence intake, it is important that we not ignore properties that already have been shown to have robust effects on eating behavior. I propose that these established determinants of intake are “The Big Three”: variety, portion size, and energy density. In general, exposure to a greater variety of foods increases intake, especially if the sensory properties of the foods differ. Variety can delay satiation by countering the hedonic decline of a food as it is consumed relative to other foods (sensory-specific satiety). Large portions also promote intake and effects of portion size persist over time and across different contexts and individuals. Among “The Big Three”, energy density likely plays the most dominant role. Even small changes in energy density influence energy intake. Unless energy density is accounted for in studies of food characteristics, it obscures other effects. This presentation will cover seminal studies on these three food properties, will introduce recent studies, and will discuss future directions.

12:00 - 1:30 PM	On Own
Lunch	

1:30 - 3:11 PM	Ballroom III
Awards Session	

1:30

Introduction

Scott Kanoski

1:32

Kathleen Keller - Hoebel Prize For Creativity, Introduction By Shana Adise

KATHLEEN KELLER

Creativity is a team effort: How transdisciplinary science can enhance understanding of ingestive behavior Science has become increasingly team-based and transdisciplinary. To be successful, we must get outside of the silos in which we were trained to learn from experts across fields, methodological approaches, and disciplines. But, does this team-based approach enhance or impede discovery? In this talk, I'll reflect on how my career in ingestive behavior has been shaped by the people and opportunities around me. I will use examples of studies from across my career to describe how the direction of my science was influenced by the context (i.e., people and environments) in which it was conducted. As a throughline to this presentation, I will discuss some foundational studies in ingestive behavior and talk about how these ideas evolved to contribute to understanding of how, what, and why children eat .

2:05

Eric Robinson - Alan N. Epstein Research Award, Introduction By Ciaran Forde

Eric Robinson

The food environment and eating ‘norms’ I will discuss data from our laboratory and others that have examined how and why the social and physical food environment influence ingestive behaviour in humans and non-human animals. I propose that the environment can exert a powerful influence on food intake because there is no objectively ‘normal’ or biologically ‘correct’ amount to eat, so what we perceive as being ‘normal’ is prone to environmental influence.

2:38

Helen Raybould - Distinguished Career Award, Introduction By Will De Lartigue

Helen Raybould

3:15 - 4:15 PM	Ballroom III
Business Meeting	

Agenda:

President's Report

Secretary/Membership Report

Treasurer Report

Long Range Planning; ½ Report

Program Committee Report

Public Communications Committee Report

New Investigator Advisory Board Report

Diversity Committee Report

Outreach Plan Proposal

4:30 - 5:30 PM	Columbus AB (Lobby Level)
NIAB - Meet the Scientist	

This event will offer new investigators the opportunity to meet and network with established scientists. We ask new investigators to sign up for this event using the following link:

https://docs.google.com/forms/d/e/1FAIpQLSfJk1b5PS_8LbiIdRYtzF5x5UUhIPMAUaLNJx8Hbs3MgumV7w/viewform?usp=sf_link.

7:30 - 11:00 PM	Ballroom IV-V
Closing Banquet & Awards Ceremony (Full Registration Required)	