32nd Annual Meeting of the Society for the Study of Ingestive Behavior

Printable Program and Abstracts

July 28 - August 1, 2025
Oxford, United Kingdom

Monday, July 28, 2025

1:00 - 3:00 PM	Boardroom
SSIB BOARD MEETING (INVITATION ONLY)	

1:00 - 5:30 PM	Registration - South Mezzanine
Registration	

3:45 - 5:00 PM	L1
MARS Lecture 1 - Sadaf Farooqi, University of Cambridge	

Chair(s): Suzanne Appleyard

P1 3:45 **Opening Greetings**
Mitch Roitman
SSIB President

P2 4:00 **Neural Regulation Of Human Appetite**
Sadaf Farooqi
University of Cambridge, , *, United Kingdom

Using genetic approaches, we have shown that disruption of multiple genes in the leptin-melanocortin pathway can cause human obesity. These molecules regulate signaling through hypothalamic circuits which project widely throughout the brain. By coupling genetic, molecular and physiological studies we are discovering key regulators of human eating behaviour. Some of these molecules regulate anxiety/fear responses, social interaction and maternal care, demonstrating the critical role of these circuits in human innate behaviour.

5:00 - 6:30 PM	South Mezzanine
Opening Reception & Exhibits	

Tuesday, July 29, 2025

8:00 - 5:30 PM	Registration - South Mezzanine
Registration	

9:00 - 10:00 AM	North & South Mezzanines
Poster Session 1, Exhibits & Coffee Break	

Poster numbers 100-146 are located in the South Mezzanine. Poster numbers 147-184 are located in the North Mezzanine.

P101 **Ingestive Behaviors Of Hard And Soft Foods As Assessed By Video Analysis And Universal Eating Monitor**

Adeleke J Akinkurolere[1], Nathan DeSalvo[2], Walls Theodore[2], Edison Thomaz[3], Cody J Arvonen[3], Dawei Liang[3], Kathleen J Melanson[1]

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Food texture influences oral processing, eating rate (ER, g/mins), and food intake (FI, g); hard foods (HF) tend to encourage slower ER than soft foods (SF). Although texture affects ER, the precise relationship between ER and FI is still unknown. Identifying this link will enable formulation of foods and guidelines to slow ER. The primary hypothesis is that SF will show faster ER and higher FI compared to HF. Secondary hypothesis is that ER and FI will be related to chewing frequency (CF, chews/min), bite size (BS, g), biting frequency (BF, bites/min), and total course duration (TCD, mins). Healthy adults ate a 4-course *ad libitum* meal of SF and HF during an individualized controlled laboratory visit. Rice and beans and churros were SF, while corn chips with chunky salsa and baby carrots represented HF. Video annotation recorded CF and a universal eating monitor recorded ER, BS, BF, and TCD. Pre and post meal weights measured FI. Statistical analysis included paired t-tests to examine differences in ER and FI while Spearman's correlation examined associations of CF, BS, BF, and TCD for SF and HF. This preliminary analysis is anticipated for a total of N=30. The sample included 9 adults (77.8% female) ages 19-33 (M=23.4±4.6), BMI (M=26.2±3.6 kg/m², range: 20.6-32.5 kg/m²). Paired t-test showed faster ER with SF than HF (d=-1.31, M=+8.27, p=0.004) along with higher FI (d=+0.89, M=+50.94, p=0.029) and BS (d=+1.27, M=+7.20, p=0.005) compared to SF. SF and HF CF were positively correlated (r=0.933, p<0.001) while HF and SF TCD were negatively correlated (r =-1.000, p=0.01). During HF consumption ER, FI, and BS were lower compared to SF. Ingestive behaviors tended to track similarly within individuals for SF and HF. This will be addressed in larger diverse samples.

P103 **The Impact Of Nutrition Labels On Japanese Consumers' Visual Attention: A Comparison Of Nutri-Scoreand Multiple Traffic Lights**

Masami Asakawa, Masao Okano
Bunkyo University, Chigasaki, Japan

This study examined visual attention to two types of front-of-pack nutrition labels, Nutri-Score and Multiple Traffic Lights(MTLs), to determine their effectiveness in attracting consumer attention. This study investigated whether consumer characteristics, such as health consciousness, influence attention patterns. Thus, the following hypotheses were tested: 1. Nutri-Score attracts attention faster than MTL. 2.Nutri-Score requires fewer total fixations than MTL. 3. Health consciousness does not affect fixation counts for Nutri-Score. 4. Health-conscious consumers exhibit more fixations on MTL compared to non-health-conscious consumers. An eye-tracking experiment was conducted on 36 university students. Participants were divided into two groups: One viewed five types of packages with Nutri-Score labels, the other viewed five types of packages with MTL labels, and their gaze data were recorded. After the experiment, the participants completed a questionnaire on food selection criteria (Steptoe, Pollard & Wardle, 1995). In the gaze data analysis, the time to first fixation and total fixation count were calculated for areas of interest on the Nutri-Score and MTL labels. A Mann-Whitney U test revealed that Nutri-Score attracted attention significantly faster than MTL for healthy products. Nutri-Score also required fewer fixations across most product types. For MTL, health-conscious participants exhibited higher fixation counts for unhealthy products than non-health-conscious participants, supporting Hypothesis 4. However, no significant differences in fixation counts were observed for Nutri-Score between health-conscious and non-health-conscious participants, rejecting Hypothesis 3.

P105 **Systematic Review And Meta-Analyses On The Effects Of Aspartame On Glucose, Insulin And Appetite-Regulating Hormone Responses**

Lucy Boxall[1], Fatemeh Eskandari[1], Julie Wallis[1], Aleksandra Bielat[1], Katherine Appleton[1]

[1]Bournemouth University, Bournemouth, United Kingdom, [2]Bournemouth Univrersity, Bournemouth, United Kingdom

Rationale: The actions of aspartame on appetite-regulating activities remain controversial, with implications for appetite- and intake-related health conditions. We aimed to identify and summarize all existing studies investigating an effect of aspartame on appetite-regulating hormone responses. **Hypothesis:** No effects will be found. **Species:** Humans. **Number of Studies:** 101 articles detailing 100 experiments. **Procedures:** We used standard systematic review processes: 1) protocol registration (PROSPERO ID: CRD42024540781); 2) searches of five academic databases, four trial registries, additional sources; 3) title, abstract and full-text screening; 4) data extraction and combination. **Results:** Searches were completed

from June – Sept. 2024, to result in identification of 101 articles, detailing 79 acute (<1 d), 8 medium-term (2–30 d) and 13 long-term (>30 d) experiments, with wide variation in aspartame provision and comparator/s. Meta-analyses of acute crossover studies revealed little to no effects of aspartame on glucose or insulin responses when compared with vehicle or other low-calorie sweeteners (LCS), and lower blood glucose and insulin levels when compared with sugars, other carbohydrates or nutritive elements. Over the medium-term, effects were reduced and inconsistent. In the long-term, no effects of aspartame were found, but high heterogeneity between studies remained. Comparable effects were found in healthy adults and in those with aspartame sensitivity or compromised glucose metabolism. **Conclusions:** Our findings suggest little to no effects of aspartame consumption on glucose metabolism over the short- or longer-term. Further studies over the long-term, investigating a range of appetite-regulating hormones, and comparing aspartame with other LCS would be of value.

P107 **Why Do Unprocessed Meals Limit Energy Intake? New Insights Drawn From Hall Et Al., 2019**

Jeffrey M. Brunstrom[1], Mark Schatzker[2], Peter R. Rogers[1], Amber B. Courville[3], Kevin D. Hall[3], Annika N. Flynn[1]

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In 2019, Hall et al. reported that participants (*N*= 20) consumed 508 kcal more per day when offered *ad-libitum* access to ultra-processed versus unprocessed meals. In this post-hoc analysis, we focused on specific 'meal components' (*e.g.*, 'sausages' and 'potatoes') that were selected and how this limited energy intake in the unprocessed meals. Two key outcomes are reported. First, selected unprocessed lunch and dinner meal components tended to have a less-equal blend of energy derived from fat and carbohydrate (lunch, $p<0.0001$; dinner, $p<0.0001$), and thus formed meals that were also of a less equal blend than those in the ultra-processed diet (lunch, $p<0.001$; dinner, $p<0.001$). This is potentially important because evidence shows the balance of carbohydrate and fat can impact the 'energy-to-satiety ratio,' which is associated with meal size. Second, when offered the unprocessed diet, participants ate surprisingly large amounts of low energy-dense meal components (<1.0 kcal/g, mostly fruit and vegetables) and thereby consumed meals that were lower in energy, ($p<0.001$), yet also significantly larger (57%) by mass ($p<0.001$). Had participants avoided these low-energy-dense unprocessed components, we suspect they would have eventually developed micronutrient deficiencies. Thus, we present a novel interpretation - unprocessed meals may cause 'micronutrient deleveraging' – a form of 'nutritional intelligence' whereby a compromise is struck between consuming meal components delivering primarily calories and those providing primarily micronutrients. Together, both factors explain 60.4% of the variance in *ad libitum* meal-energy intake across both diets. Given the implications for our understanding of energy balance, researchers might consider not only the negative aspects of ultra-processing but also the benefits of consuming an unprocessed diet, which are not well understood.

P111 **Early Brain Structure Predictors Of Eating In The Absence Of Hunger In Preschool Children**

Abdul Ibrahmim[1], Elena Jansen[1], Angelica Owen[2], Rosa Cano Lorente[2], Jennifer Beauchemin[2], Muriel Bruchhage[2], Daphne Koinis-Mitchell[2], Viren D'Sa[2], Sean Deoni[2], Susan Carnell[1]

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Eating in the absence of hunger [EAH] is associated with higher BMI and later weight gain in preschool children. Eating behavior is the output of brain circuits that develop rapidly in early childhood, but neural substrates underpinning human appetite variation in early life are not understood. We therefore recruited n=32 3-5y olds (17F, 15M) (mean±SD 4.4±0.5y) from RESONANCE, an MRI cohort study beginning in infancy, to complete an EAH test. Participants were presented with a snack array for 10 min, following a standardized meal. We leveraged previously-collected and processed MRI data acquired 1.2-17.9mo (7.1±4.6mo) before the EAH test. Sex-stratified sets of multiple regression models analysed relationships of volumes of bilateral brain regions within frontal cortex (9x2=18 ROIs), striatum (4x2=8 ROIs), and other appetite-associated regions (amygdala, hippocampus, insula, 3x2=6 ROIs), with EAH intake (0-464.0, 166.5±130.3 kcal), controlling for intracranial volume, time between MRI and EAH, and prior meal intake (111.8-1756, 631.7±340.9 kcal). FDR-corrected analyses demonstrated that, in males, lower volumes in 8/9 right frontal cortex ROIs were associated with higher EAH intake. Uncorrected analyses additionally showed that, in females, higher left hippocampus and right insula volumes were associated with higher EAH intake. Left frontal, and bilateral striatum and amygdala ROI volumes, were unassociated with EAH intake. These preliminary findings suggest early structural development of brain appetite circuits may predict later eating behavior.

P113 **Sweet Sensations At Home: Developing An At-Home Sensory Test To Explore Sweet Liking And Sensitivity In Type 2 Diabetes**

Tobias Long[1,2], Alison Smith[1], Margaret Thibodeau[1], Elizabeth King[1], Sally Eldeghaidy[1,2], Qian Yang[1]

[1]School of Biosciences, Sutton Bonington Campus, University of Nottingham, Nottingham, United Kingdom, [2]Sir Peter Mansfield Imaging Centre, University Park, University of Nottingham, Nottingham, United Kingdom

Dietary guidelines worldwide recommend reducing dietary free sugars, particularly for people with type 2 diabetes (T2D). It is well reported that there are individual variations in sweet liking and taste sensitivity. Limited research has investigated how these characteristics affect dietary intake and eating behaviour, especially in individuals with or at risk of T2D. Large-scale studies are needed to examine these relationships, however, recruiting understudied populations is challenging, and there is a need to develop testing methods that do not require central-location sensory testing. To address this, a series of five pilot experiments (n=7-42) were conducted in healthy adults to develop and test a home-use sensory testing kit. Samples in the kit needed to be stable during delivery, easy for participants to self-administer with limited supervision, and to yield comparable results to central-location testing. The final kit included four sweet solutions (3, 12 and 36% w/v sucrose and 4.5% w/v sucralose-based sweetener) to measure sweet-liking status and ten paper taste strips to capture differences in supra-threshold responsiveness to the five basic tastes at two concentrations. Participants, supervised remotely through online meetings , accessed an on-screen questionnaire that guided them through the test procedures while also capturing various aspects of eating behaviour. Results will be presented evaluating the ease and replicability of the home testing procedure. Insights into how individual sensory traits relate to aspects of eating behaviour will also be discussed. This home-based sensory testing procedure, which reduces participant burden, could increase participation in future sensory research among understudied populations.

P115 **Prenatal And Early-Life Stress Predicts Eating Behaviors In Young Children**

Ying Meng[1], Thomas O'Connor[2]

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Rationale: Prenatal and early-life factors influence brain development, including the hypothalamus. Cross-sectional studies link stress and cortisol levels to eating behaviors in children and adolescents, but whether prenatal and early-life stress and cortisol directly shape eating behaviors remains unclear. Hypothesis: We hypothesized that prenatal and early-life stress exposure and physiology are associated with eating behaviors, such as satiety responsiveness, food fussiness, and food preference. Methods: This pregnancy cohort study included 162 mother-child dyads with eating behavior assessed at 36 months using the Child Eating Behavior Questionnaire and Preschool Adapted Liking Survey. Maternal depression, anxiety, and stress were measured at each trimester (n≤144), along with diurnal cortisol levels (n≤109). Child cortisol response to stressors was assessed at 6 and 12 months (n≤127). Multivariable linear regressions were conducted adjusting for maternal and child factors. Results: Maternal depression (2nd/3rd trimester) and perceived stress (3rd trimester) were positively associated with emotional overeating. Maternal depression (2nd trimester) and perceived stress (3rd trimester) correlated with higher satiety responsiveness. Depression and anxiety across all trimesters increased food fussiness risk, while maternal anxiety was linked to lower vegetable liking. Higher maternal cortisol AUC (1st/2nd trimester) was associated with less food fussiness, and infant cortisol AUC (6 months) correlated with lower vegetable liking. Conclusion: Findings support the hypothesis that prenatal and early-life stress influence child eating behaviors.

P117 **Ability To Predict Irregular Periods Of Food Deprivtion Improves Body Weight Regulation In Starlings**

Charlotte Parker, Ryan Nolan, Clare P. Andrews, Melissa Bateson
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Food insecurity is associated with higher body weight in humans and other species, but the causal effect of unpredictability in food availability on weight gain is unknown. We measured food intake and body weight in European starlings (*Sturnus vulgaris*; n = 16) exposed to 16, repeated, 5-hour periods of food deprivation scheduled irregularly over 32 days. A 1-hour visual cue, that either reliably preceded (Predictable group) or was uncorrelated (Unpredictable group) with food deprivation was used to manipulate the predictability of deprivation. During the cue, Predictable birds spent less time perched inactive and reduced their food intake, indicating that they had learned the contingency. Despite this, they lost less weight during deprivation. They also ate less and gained less weight on the next *ad libitum* day. Birds with the largest behavioural response to the cue had the lowest overall variance in body weight. Consistent with the insurance hypothesis, daily food intake and body weight increased over time in both groups and mean body weight was higher in the Unpredictable group. Our results suggest that when food deprivation was predictable, the birds were less reliant on stored fat and instead used cognitively mediated, short-term hypometabolism to mitigate the effects of food deprivation. These findings contribute to our understanding of the biological impacts of food insecurity and support the hypothesis that unpredictable food deprivation disrupts homoeostatic regulation of body weight. We discuss the implications of our findings for the differential health impacts of food insecurity and intermittent fasting.

P119 **Recognising Infant Appetite Cues During Mealtimes And Its Association With Caregivers&Rsquo; Ability To &Ldquo;Tune-In&Rdquo; To Their Own Internal Satiation And EmotionS.**

Shihui Yu, Alison Fildes, Pam Birtill, Tang Tang, Marion Hetherington
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Caregivers vary in recognising and responding to infant hunger, appetite, and satiety cues with potential consequences for responsive feeding (RF). Three studies were designed to investigate individual differences in recognising infant appetite cues during mealtimes and their link to RF. We hypothesised that individual differences in "tuning-in" to one's own internal cues would influence recognition and response to infant cues. Study 1 tested recognition accuracy of infant appetite cues in adults (n=198) online using 10 video clips of infants at the start and end of a meal. Recognition scores were high, but alexithymia correlated with low recognition (r=−.15, p=.03). In Study 2, hierarchical regression showed caregivers (N=445) who "tune-in" to internal cues scored high on recognising infant appetite during feeding (p<.001). Caregivers with alexithymia reported lower scores in recognising infant appetite cues (p<.001) and fewer positive mealtime emotions (p<.001), compared to those without alexithymia. Structural equation modelling showed that caregivers' ability to "tune in" to their own internal satiation cues mediated the link between alexithymia and their infant appetite recognition. Study 3 included one-to-one semi-structured, video-elicited interviews with 12 mothers and 2 fathers from Study 2 who had scored high on alexithymia. Thematic analysis of interview data revealed mealtime challenges and stress experienced by caregivers also the effect of context on how meals were managed. Overall, these 3 studies illustrated that the ability to "tune-in" to internal cues predicted RF practices and mealtime emotions. Future research could explore tailored support to promote RF practices and positive mealtime experiences.

P121 **Circulating Agouti-Related Peptide Is A Reproducible Measure And Correlates Negatively With Age**

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Circulating Agouti-related peptide (cAgRP) has been proposed as a marker of hypothalamic melanocortin activity, a key controller of feeding. In rats, cAgRP correlates with hypothalamic AgRP expression. In humans, cAgRP varies with fasting and feeding similarly to cAgRP expression in the rodent hypothalamus, and increases with weight loss. We examined the reproducibility and baseline determinants of cAgRP in adults with obesity. We enrolled 17 subjects (age 39±9 years, BMI 37±6 kg/m^2, 82% women) in a 6-month lifestyle-based weight loss intervention study. cAgRP, leptin and insulin were assayed in fasting conditions at baseline and 2 months later (visit 2, V2) with commercially available assays. Reproducibility of cAgRP was examined by intraclass correlation coefficient (ICC). Baseline determinants of cAgRP were explored with univariate correlation and non-parametric tests. Significance was set at p<0.05. Average weight loss at V2 was 4.6±3.3% and 41% of subjects lost 5% or more of baseline weight. While high interindividual variability was seen for both baseline cAgRP and cAgRP change with weight loss (median [IQR] 78.1 [25.4] ng/ml and 2.5 [27.5]%, respectively), baseline cAgRP significantly and strongly correlated with V2 cAgRP (ICC 0.806, p<0.001). Baseline cAgRP did not differ by sex and was not associated with baseline BMI, leptin or insulin, but a negative correlation with age was present (Spearman's rho -0.49, p=0.046). Age also tended to correlate positively with cAgRP change from baseline to V2 (Spearman's rho 0.47, p=0.06). Our preliminary results suggest that cAgRP levels may be a reproducible trait. Single nucleotide polymorphisms

(SNP) in the AGRP gene have been reported. Future studies should investigate whether these SNP influence fasting cAgRP levels.

P123 **How We Sense Fullness After A Meal - Molecular Mechanisms Of Vagal Gut Mechanosensation**

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Mechanical forces generated during food intake and digestion are detected by the gut and relayed to the brain to promote satiety and suppress further consumption. However, the cellular and molecular mechanisms underlying this mechanosensory signaling remain poorly defined. We hypothesized that distinct subpopulations of gut-innervating vagal afferents mediate fullness through specialized mechanosensory responses. Results: Using in vivo calcium imaging during graded intragastric balloon distension, we identified vagal afferents that respond robustly to gastric stretch in a dose-dependent manner. These mechanosensitive neurons are genetically heterogeneous and using machine learning we identified five distinct response profiles to stretch. To resolve this heterogeneity, we combined in vivo functional imaging with multiplexed fluorescent in situ hybridization. This revealed that at least three ion channels—Piezo1, Piezo2, and TRPA1—define non-overlapping subtypes of vagal afferents, each associated with distinct sensory dynamics. These channels may function as putative mechanoreceptors, though their roles remain to be confirmed. Ongoing studies are testing the necessity of neurons expressing these markers in feeding behavior. Conclusions: Our findings suggest that the sensation of fullness arises from integrated activity across genetically distinct vagal subtypes and lay the groundwork for targeted manipulation of gut-brain circuits to regulate feeding.

P125 **Acute Exercise Modulates Brain Insulin Sensitivity In Men With Normal Weight**

Anja Bierenstiel[1,2], Patrick Schneeweiss[4,5], Ralf Veit[1,2], Theresa Ester-Nacke[1,2], Leontine Sandforth[1,2,3], Kim Wacker[1,2], Judith Ahrens[1,2], Reiner Jumpertz-von Schwartzenberg[1,2,3], Andreas Niess[4,5], Andreas L. Birkenfeld[1,2,3], Hubert Preissl[1,2,3], Cora Weigert[1,2,6], Stephanie Kullmann[1,2,3]

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Brain insulin resistance impairs cognition, reward processing, and energy balance, linked to obesity, type 2 diabetes, and Alzheimer's disease. Building on previous research showing improved brain insulin responsiveness after eight weeks of aerobic exercise, this study examines the acute effects of a single exercise session at varying intensities on brain insulin action. In an ongoing study, eleven men with normal weight (body mass index range: 20.14 to 24.46 kg/m²; age range: 20 to 50 years) were enrolled in a randomized, placebo-controlled crossover design. Participants attended three separate visits for 43 minutes of high-intensity interval training (HIIT), 60 minutes of moderate-intensity continuous training (MICT) and a 60-minute passive control. Brain activity was assessed one hour post-exercise or control condition using functional magnetic resonance imaging, analyzing cerebral blood flow (CBF) before and after intranasal insulin spray with a flexible factorial model adjusted for global CBF. Statistical significance was determined using family-wise error correction ($p \leq 0.01$) with small volume correction for insulin-sensitive brain regions. Post-exercise CBF was significantly higher in the hippocampus and putamen compared to control. A significant interaction between exercise condition and insulin spray was observed, showing a decreased response to intranasal insulin in the amygdala, putamen, and substantia nigra after exercise compared to control. This did not differ between intensities. This preliminary data suggests that a single bout of exercise in men with normal weight affects insulin action in limbic-striatal regions. Further research is needed to determine whether this response is a predictor for long-term effects of physical exercise.

P127 **Exercise Alters Gut To Brain Signals That Reduce Sugar Consumption**

Lavinia Boccia[1], Giulia Uhr[2], Jo Lewis[3], Lenka Donhalova[2], Irene Caffa[4], Luca Tagliafico[4], Heather Collins[5], Myrtha Arnold [6], Alessio Nencioni[4], Fiona Gribble[3], Frank Reimman[3], Christoph Thaiss[2], J. Nicholas Betley[1]

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The rise in obesity and high-sugar diet consumption has intensified global health concerns, necessitating more effective interventions. Among these, exercise training has positive effects on multiple aspects of well-being, such as enhanced cardiovascular health, improved metabolic function, cancer prevention and control, aging, and mental health. Growing evidence also suggests that exercise influences dietary habits, encouraging the adoption of healthier food choices. This correlation has attracted significant attention, driven by observations that regular exercise can lead to a decreased preference for highly palatable diets, especially sugary foods. Despite these findings, the mechanisms underlying this shift in dietary preferences remain unclear. We hypothesize that these shifts might be driven by hardwired biological mechanisms rather than a conscious decision to eat healthier. We observe that exercise training leads to a dramatic reduction in sugar consumption in rodents and humans. These changes are mediated by changes in gut-brain signaling that reinforce sugar. Routine exercise leads to microbiome and metabolites changes that elevate levels of Glucose-dependent Insulinotropic Polypeptide (GIP). These exercise-induced changes in body physiology are sufficient to reduce sugar consumption, decrease the dopamine response to sugar in the gastrointestinal (GI) tract, and lower the motivation to obtain sugar. Taken together, these studies map an exercise-induced sensing pathways that leads to changes in macronutrient consumption that occur in

exercise-trained individuals. These findings not only enhance our understanding of the gut-brain axis but also open the way for developing innovative strategies to address diet-related health challenges.

P129 **Ventral Tegmental Area-To-Cerebellum Connectivity Is Disrupted In Acute Anorexia Nervosa**

Liuyi Chen, Sarah H. Guo, Arnold Bakker, Angela Guarda, Kimberly R. Smith
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Anorexia Nervosa (AN) is a severe mental and behavioral health disorder characterized by altered reward processing and maladaptive eating behaviors. Our previous research has shown that individuals with AN experience reduced food reward relative to healthy controls (HC), with lower food liking and wanting when they are acutely ill. However, the neurobiology underlying reward deficits in AN remains poorly understood. Preclinical evidence indicates that the deep cerebellar nuclei play a critical role in modulating the phasic dopamine response to food reward in the ventral striatum. Recent diffusion tractography studies in humans identified a structural connection between the cerebellum and ventral tegmental area (VTA), a midbrain structure that houses dopamine neuron cell bodies crucial for reward processing. It remains unclear whether this cerebellum to VTA connection is functionally connected and, if so, whether this connectivity is altered in individuals with acute AN. In this study we employed 3 Tesla resting-state functional magnetic resonance imaging (rs-fMRI) to assess the functional connectivity between the cerebellum and VTA in 54 HC women and 20 women with acute underweight AN following an overnight fast. Analysis was performed using the CONN toolbox, revealing significant cerebellum-VTA functional connectivity in HC (uncorrected $p<0.001$) but not in AN (uncorrected $p = 0.913$). A significant difference in connectivity between the groups was observed (uncorrected $p = 0.0496$). These preliminary findings suggest that a functional cerebellum-VTA connection is present in HC but disrupted in acute AN. Given the emerging role of the cerebellum in cognitive and affective regulation, these findings highlight a potential neural basis for maladaptive eating behaviors in AN.

P131 **Sex Dependent Food Reward In Mice**

Asia Dofat, Tüng Bui, Keyrstin Jacobs, Rachelle Jacob, William Howe
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Recent evidence suggests that post-ingestive gut signals modulate midbrain dopamine (DA) systems to influence food reward. It has also been suggested that biological sex may also influence macronutrient preference and intake, yet its relationship with post-ingestive reward signals has not been explicitly studied. Here, we tested the hypothesis that sex differences in food reward stem from differential modulation of the afferent pathway linking gut nutrient sensors to midbrain dopamine centers. To this end we used a free-choice paradigm to track preference for fats, carbohydrates, or combinations of the two, in male (n=12) and female (n=11) mice over 14 days. Results showed that females show increased consumption of fat compared to other macronutrients and compared to male fat intake. Within the female group, carbohydrate intake, but not fat, varied significantly across the estrous cycle, specifically increasing during estrus compared to diestrus. To examine the relationship between these preferences and post-ingestive modulation of the midbrain, we examined neural activation in response to intragastric infusion of fat, carbohydrate, combo, or a PBS control in males (n=11) and females (n=11). Here, we noted a dissociation in the impact of fat containing macronutrient infusions in the SNc, but not VTA, of males and females. Given previous studies detailing differences in peripheral expression of PPAR-a, a nuclear receptor necessary for fat reinforcement, ongoing studies quantify PPAR-α protein levels across the stomach and gut tissue of males (n=13) and females (n=17 female). Together, these studies aim to illustrate a mechanism underlying sex differences in food preference.

P133 **Interplay Of Norepinephrine (Ne) And Neuropeptide Y (Npy) In The Integration Of Visceral Afferent Information By Catecholamine (Ca) Neurons Of The Nucleus Tractus Solitarius (Nts)**

Luciano G Fernandes, Minyang Zhu, Eric T Winzenried, Rowan J Calkins, Suzanne M Aplleyard
Integrative Physiology and Neuroscience Department, Washington State University, Pullman, WA, United States

Catecholamine (CA) neurons in the nucleus tractus solitarius (NTS) integrate vagal afferent signals from the gastrointestinal (GI) system. These neurons then relay this information to downstream brain regions to influence food intake. Interestingly, some NTS-CA neurons co-express NPY. In addition, the NTS receive projections from the ventrolateral medulla (VLM) catecholamine neurons that also express both NPY and norepinephrine (NE). However, the effects of NE itself and how it interacts with NPY to modulate NTS catecholamine neurons is unknown. In this study we recorded from catecholamine neurons identified using transgenic mice expressing EGFP under the control of the tyrosine hydroxylase promoter (TH-EGFP) while stimulating the solitary tract (ST) that contains the incoming vagal afferents. As shown previously the vast majority of TH-EGFP neurons are directly activated by incoming afferents (average EPSC amplitude: -580±120 pA). NE significantly reduced the amplitude of these ST-EPSCs in 88% of TH-EGFP neurons (10uM: 68±0.04 % of control, n = 23 and 30uM: 68±0.06 % of control, n = 15). This was through activation of the alpha2 adrenergic receptor as it was mimicked by alpha2 adrenergic receptor agonists and blocked by alpha2 adrenergic receptor antagonists. NPY (100 nM) similarly decreased ST-EPSC amplitude (69±0.08 % of control, n = 4) in 100% of TH-EGFP neurons. Moreover, co-administration of NE and NPY significantly reduced ST-EPSC amplitude (47±0.08 % of control, n = 7). Taken together, these results suggest that NE and NPY interact presynaptically to inhibit vagal activation of NTS-CA neurons.

P135 **The Locus Coeruleus Calcitonin Receptor Can Be Engaged By Amylin And Calcitonin Gene-Related Peptide To Suppress Feeding Without Inducing Nausea**

Samantha Fortin, Marcos Sanchez-Navarro, Maggie Zhou, Jiayin Hu, Carlie Zhang, Brandon Alonso, Matthew Hayes
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Efforts to fully characterize the diversity of mechanisms underlying energy balance control have led to the identification of atypical sites of action for metabolic signals. The locus coeruleus (LC), the major noradrenergic nucleus of the brain, has recently been shown to regulate food intake and energy expenditure. Here, we use complementary pharmacological, behavioral, immunohistochemical and genetic approaches in rats and mice to demonstrate a role for LC calcitonin receptors (CTRs) in feeding behavior. LC neurons robustly express CTRs that can be pharmacologically and chemogenetically activated to potently inhibit food intake and body weight. In contrast to the anorexia following LC glucagon-like peptide-1 receptor signaling, engagement of LC CTRs does not induce nausea or changes in autonomic physiology including heart rate, body temperature and gastric emptying. We next examined the ability of amylin and calcitonin gene-related peptide (CGRP), two endogenous anorectic signals that signal through the CTR, to modulate feeding through signaling in the LC.

RNAscope analysis revealed that LC CTRs are capable of responding to amylin and CGRP, as they co-express RAMP1, and indeed, microinjections of either peptide to the LC induces anorexia without nausea. Current work is aimed at examining the translational relevance of LC CTRs to the weight loss induced by amylin analog therapies (i.e. cagrilintide, eloralintide) being developed for obesity treatment.

P137 **Hungry Vs. Sated: Brain Activation During Food Consumption In Children**

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While fMRI has improved characterization of neurocircuitry involved in ingestive behavior, its sensitivity to motion precludes data collection while children are eating. In contrast, functional near-infrared spectroscopy (fNIRS) is more tolerant to motion, making it an ideal approach to examine neural activation during food consumption. As part of a longitudinal study, 52 children (9-11-years; 18 male) completed fNIRS during a taste-test after a 3-hour fast (fasted) and after consuming an *ad libitum* meal (sated; chicken nuggets, pasta, and grapes). Small samples (~2g) of 9 meal and non-meal foods ranging in energy density were given to taste during fNIRS. For each food, children rated how much they wanted to eat it and were then instructed to consume it and rate how much they liked it. Group models tested the difference in frontal and temporal neural response to tasting meal foods when fasted compared to sated using a mixed effects model with participants treated as a random effect and Benjamini-Hochberg correction for multiple comparisons. Children show greater activation during intake of meal foods when fasted compared to sated in right orbital frontal cortex and bilateral temporopolar, inferior frontal gyrus, supplementary motor cortex, and frontal eye-fields. In contrast, there was greater activation when sated compared to fasted in bilateral frontopolar and dorsolateral prefrontal cortex (PFC). Therefore, children engaged regions related to valuation and motor planning when tasting foods while hungry but engaged regions related to inhibitory control when tasting foods while sated. This was the first to use fNIRS to assess neural activation during solid food intake in children, laying the foundation for using fNIRS during ecological feeding paradigms (e.g., meals).

P139 **Structural Brain Differences In Metabolically Healthy And Metabolically Unhealthy Obesity In The Uk Biobank Sample**

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Obesity is one of the top modifiable risk factors for Alzheimer's disease. It exerts negative effects on the brain primarily through metabolic pathways. Recently, the term 'metabolically healthy obesity' (MHO) was coined to describe people with phenotypic adiposity (body mass index [BMI] > 30 kg/m^2) but with no major metabolic comorbidities. In this study we set out to investigate structural magnetic resonance imaging brain and cognitive differences between individuals with MHO and metabolically unhealthy obesity (MUO). We defined MHO as individuals with phenotypic obesity, normal systolic blood pressure (<130mmHg), no blood pressure medication, and no type 2 diabetes diagnosis. We used a subsample of 2558 age-, sex-, and BMI-matched individuals from the UK Biobank (n=1279/group; average age=61+-7 years; ~35% females; BMI=33+-4kg/m^2). With linear regression, we investigated cerebral cortical thickness, surface area, white matter integrity, as well as volume and cellularity of subcortical brain structures. We also tested cognition in 6 domains, including working memory or fluid intelligence. The MHO group exhibited a better overall metabolic profile compared to the MUO group on measures that were not used as group inclusion criteria, e.g. levels of HbA1c or HDL. The MHO group had higher cortical thickness and surface area in the fronto-temporal cortices, paralleled by higher measures of cellularity and volume in the hippocampus, caudate nucleus, and thalamus, as well as better overall white matter integriy (p_{FDR}<0.05), suggesting a lower degree of neurodegeneration. No group differences in cognitive measures were found. These findings suggest that obesity should be examined beyond anthropometric measures alone, highlighting implications for both clinical practice and future research directions.

P141 **Cck-Sensitive Vagal Afferents Activate Nts^{Npy} Neurons.**

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Vagal afferents carrying information from the gut terminate in the nucleus of the solitary tract (NTS), and NTS neurons then process and relay this information to other brain regions involved in the control of food intake (FI). Activation of most NTS neurons inhibits FI, including broad activation of NTS catecholamine (CA) neurons. However, small subpopulations of CA neurons promote FI, including neurons that express neuropeptide Y (NTS^{NPY} neurons). Here, we determined how NTS^{NPY} neurons are connected to incoming vagal afferents and which type of afferents modulate their activity. We performed voltage clamp recordings from brain slices containing the NTS and incoming vagal afferents in the solitary tract (ST) from male and female mice. NPY neurons were identified by crossing NPY-IRES-Cre and Rosa-loxP-tdtomato mice. 86% of NTS^{NPY} neurons had monosynaptic connections to the solitary tract, with an average ST-evoked excitatory post-synaptic current (ST-EPSC) of -230.15±20.15pA and paired-pulse ratio of 0.55±0.20, n = 28 cells) at 50Hz stimulation. Cholecystokinin (sulfated-CCK-octapeptide, 100nM) caused a 5.3±0.9-fold increase in frequency of spontaneous (s)EPSCs in 14/18 of cells (p <0.05). In contrast, a serotonin receptor 3 (5-HTR3) agonist (SR57227, 10μM) had no effect on sEPSC frequency (n = 8, p = 0.51). Taken together, our data suggest that most NTS^{NPY} neurons are directly activated by CCK-sensitive afferents, which respond primarily to fat and protein in the gut; but not 5-HT-sensitive afferents, which respond more to mechanical stretch of the gut. CCK-sensitive afferents are thought to promote an overall decrease in FI; however, the finding that they activate a population of neurons that promotes FI suggests that they may elicit a bimodal response.

P143 **Neural Correlates Of The Subjective Perception Of Oral Fat In Liquid Foods**

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Overconsumption of high-fat foods is a major driver of weight gain, yet the neural mechanisms linking the oral processing of fat to eating behaviour remain unclear. Here we combined novel food-engineering approaches with functional neuroimaging to show that the human oral somatosensory cortex (oSSC), anterior insula, amygdala, and hypothalamus make specific contributions to the oral-sensory perception of fat. Male and female volunteers (N=22) sampled and evaluated nutrient-controlled liquid foods varying in fat and sugar content ('milkshakes'). During oral food processing, the oSSC and anterior insula (putative primary taste cortex) made similar but partly distinct contributions to fat perception: Activity in oSSC correlated with the probability that participants reported the subjective sensation of fat, whereas insula activity correlated with the probability that this sensation correctly reflected the food's fat content. Both areas also encoded oral-sensory indicators of fat content: the foods' viscosity and oral sliding friction. Similarly, the amygdala jointly encoded subjective fat-perception, viscosity, and sliding friction. Across subjects, amygdala sensitivity to oral fat predicted aspects of fat consumption in a naturalistic eating test. The hypothalamus responded similarly to animal-based (dairy) and plant-based (soy) high-fat foods. These findings advance our understanding of how specific brain areas in the human taste and reward pathways contribute to the oral perception and consumption of dietary fat. References Khorisantono PA, Huang, FY, Sutcliffe MPF, Fletcher PC, Farooqi IS, Grabenhorst F (2023) A neural mechanism in the human orbitofrontal cortex for preferring high-fat foods based on oral texture. J Neurosci 43:8000-8017.

P145 **A Rapid Arousal Brake On Hunger Neurons And Its Release In Narcolepsy**

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Human sleep-wake disorders are often accompanied by eating disorders, but the interplay between hunger and arousal remains unclear. Pupil-linked arousal correlates with the dynamics of hypocretin/orexin (H/O) neurons, whose malfunctions link to pathologies. It is currently thought that H/O neurons activate hunger-causing agouti-related peptide (AGRP) neurons, creating concurrent arousal and hunger. Here, we directly measure pupil-linked arousal dynamics and concurrent AGRP neuron activity by using combined pupillometry and photometry and find that, instead, pupil dilations correlate with reductions in AGRP neuron activity (n = 5 mice, p=0.0079). Optogenetic H/O neuron stimulation reproduced this inhibition effect on AGRP neurons(Chrimson vs control, p=0.02; n=5 per group). Ablating H/O neurons in H/O-DTR+ mice attenuated this correlation between pupil dilation and reduction in AGRP neuron activity (n=5 per group, p=0.0086). In this mouse model of human type 1 narcolepsy, which involves unexplained overeating, we detected abnormal AGRP neuron hyperactivation during specific brain states, including the symptomatic shut-downs of arousal (n = 31 cataplexy episodes from 5 H/O neuron ablated mice, p<0.000). Finally, intact H/O neurons are required for normal food value perception by AGRP neurons(chow vs palatable food n =6 DTR-, p=0.04; n=7 DTR+,p=0.30), and for suppression eating(DTR- n = 5 vs DTR+ n = 4 mice, p= 0.002) and AGRP neurons(DTR- n = 5 vs DTR+ n = 5 mice, p= 0.01) by unexpected non-food stimuli. By demonstrating a rapid inhibitory H/O → AGRP influence and multiple pathophysiological consequences of its loss, these findings reveal a rapid functional link between arousal and hunger that is impaired by a neural defect associated with human disorders.

P147 **Evaluating Dhea Administration As A Preclinical Model Of Pcos: Diagnostic And Nondiagnostic Effects On Metabolism, Cognition, And Neurophysiology**

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Polycystic Ovary Syndrome (PCOS) is the most common reproductive disorder in pre-menopausal women, yet it remains under-researched and poorly understood. Preclinical PCOS models often use androgen administration to mimic the hyperandrogenic state observed clinically. Dehydroepiandrosterone (DHEA), the most abundant circulating androgen in humans, is commonly used, but its reliability in inducing PCOS-like symptoms in rodents has been inconsistent. Here, we assessed DHEA's validity as a PCOS model in female Long Evans rats (N = 25), focusing on behavioral, cognitive, and neurophysiological outcomes. Rats received daily subcutaneous injections of either DHEA or sesame oil and were given access to a 10% fructose solution (an external obesity factor) or water, yielding four groups; separate homecage controls received no manipulation. We hypothesized that DHEA would induce both diagnostic and non-diagnostic PCOS-like symptoms, with fructose intake exacerbating effects. However, metabolic data showed minimal group differences, including no evidence of insulin resistance or hyperadiposity, nor effects on anxiety-like behavior or spatial working memory. Despite the absence of common non-diagnostic symptoms, DHEA-treated animals met Rotterdam Criteria for PCOS diagnosis; these females exhibited disrupted estrous cycles and elevated testosterone levels, regardless of fructose intake. Thus, while DHEA produced diagnostic PCOS-like features, this model may not capture the full range of metabolic and behavioral alterations seen in humans.

P149 **Diet-Induced Enhancements Of Medium Spiny Neuron Synaptic Responsivity In Nucleus Accumbens Of Adult Rats**

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Over-consumption of sugary, fatty foods leads to obesity and contributes to metabolic syndrome. In rodents, eating a "junk-food" (JF) diet increases AMPAR-mediated excitatory transmission in the nucleus accumbens (NAc) core of obesity-prone but not obesity-resistant rats. However, it is unclear whether JF diet also enhances responsivity (i.e., membrane depolarization) of NAc neurons to excitatory drive. Thus, here we used electrophysiological approaches to study the net effect of JF diet consumption on the ability of excitatory glutamate inputs to drive activity of NAc medium spiny neurons (MSNs) and to determine the contribution of different types of glutamate receptors to this excitation. Briefly, adult obesity-prone rats of both sexes were given free access to JF for 10 days, followed by 1-2 days of free access to standard chow only; controls were given standard chow throughout. Recordings were made in coronal brain slices to assess changes in membrane potential in response to increasing electrical stimulation of the slice (input/output) and spontaneous excitatory postsynaptic currents (sEPSC). Initial results indicate that JF diet enhances the responsivity of MSNs to excitatory input in males, with no effects on sEPSC amplitude or frequency. In contrast, no changes in input/output responses were found in females, but

sEPSC frequency was enhanced by JF diet, and this effect varied with the cycle. Additional studies in controls show that membrane depolarization in response to electrical stimulation is mostly due to activation of AMPARs, with ~25% of this effect due to CP-AMPAR; analysis in JF groups is ongoing. Initial results suggest sex differences in the effects of JF diet on NAc function, with enhanced responsivity in males and more frequent sEPSC in females.

P151 **Perinatal Exposure To Maternal Western Diet Alters The Central Glp1 System In Rat Offspring**

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When rat dams consume a high-fat, high-sugar "Western Diet" (WD) during pregnancy and lactation, their offspring later display increased food reward-driven behaviors. Since food reward typically is reduced by central GLP1 signaling, we hypothesized that maternal WD exposure suppresses GLP1 signaling in offspring. We tested this using a 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 (control) or WD throughout gestation and lactation. All offspring were weaned onto chow on postnatal day 21 (P21). At P60, some offspring were injected with the GLP1R agonist Ex4 (10mg/kg) and perfused to quantify RFP+ GLP1 axons and Ex4-induced cFos (4F, 2M per rearing group), while others were moved into BioDAQ cages with access to both WD and chow (2F, 2M per rearing group). The density of RFP+ fibers and cFos+ neurons was significantly reduced in WD-reared offspring at P60, despite chow-only feeding for 5+ weeks. Further, compared to chow-reared rats, WD-reared rats initiated more WD feeding bouts and spent more time consuming WD during the first 6 hours of the dark cycle. After 4 weeks on WD, within-subjects dose-response curves for Ex4-induced hypophagia (0, 1, 3, 10, 25mg/kg) established a significant rightward shift in WD-reared rats (i.e., less hypophagia at low doses), evidence for reduced GLP1R-dependent signaling. Together, these novel data support the view that perinatal exposure to maternal WD alters central GLP1 projections and GLP1R signaling in offspring, perhaps contributing to the known effects of early-life nutrition on metabolic health and reward-driven behaviors.

P153 **Binge Ethanol Consumption Can Be Attenuated By Systemic Administration Of Minocycline And Is Associated With Enhanced Neuroinflammation In The Central Amygdala**

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Alcohol use disorder (AUD) has a complicated pathophysiology. Binge ethanol intoxication may produce long-lasting changes throughout extended amygdala neurocircuitry including neuroinflammation, often leading to relapse. Therefore, understanding the role of binge drinking induced neuroinflammation on extended amygdala neurocircuitry is critically important for treatment. We sought to understand the role of neuroinflammation using a mouse Drinking in the Dark (DID) model. In a 5-week DID paradigm, we demonstrate that acute intraperitoneal (IP) injection of the anti-inflammatory drug minocycline significantly reduced binge drinking repeatedly in male and female Cx3CR1-GFP and C57BL/6J mice (n = 44) using a 3 way RM ANOVA. Importantly, IP administration transiently decreased intermittent access sucrose consumption (n = 26), but was not observed on the second IP injection using a 2 way RM ANOVA, and did not significantly alter food or water consumption (n = 21) using a 2 way ANOVA , suggesting that minocycline may not alter long-term consumption of natural rewards. To assess neuroinflammation, we developed a novel analysis method using a Matlab image analysis script, which allows for non-biased skeletonization and evaluation of microglia morphology to determine activation states in Cx3CR1-GFP knock-in mice after repeated DID. We observed significant morphological changes of microglia within the CeA (n = 29), but no differences in the BLA (n = 18) using a one way ANOVA. Taken together, this study demonstrates repeated binge ethanol consumption can produce significant levels of microglia morphology changes within the CeA, and that immunomodulatory therapies may be an intriguing pharmacological candidate for the treatment of AUD.

P155 **Central Relaxin-3 Agonism Attenuates Cisplatin-Induced Anorexia And Body Weight Loss Potentially Through A Gdf-15 Independent Pathway**

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Cancer-cachexia is a disorder characterized by metabolic disturbances, stress and anorexia. Unfortunately, there are currently no therapeutics available to effectively combat cancer-cachexia. The relaxin-3 system has been strongly implicated in having a role in feeding and stress behaviors. Relaxin-3 producing neurons are found in the Nucleus Incertus (NI) of the brainstem, with its receptor, relaxin family peptide receptor 3 (Rxfp3), being widely distributed throughout the brain. Central administration of relaxin-3 potently increases food intake in rodents, while central Rxfp3 antagonism blocks this effect. In addition, chronic stress and repeated food restriction was associated with increased NI relaxin-3 mRNA levels and central infusion of corticotropin-releasing factor (CRF) activated NI relaxin-3 neurons. Overall, this suggests that the relaxin-3 system may promote orexigenic behaviors under stressful conditions. Therefore, we tested the hypothesis that central relaxin-3 can attenuate cisplatin-induced cachexia. Notably, intracerebroventricular (ICV) administration of relaxin-3 attenuated systemic cisplatin-induced anorexia and body-weight loss in rats without attenuating its nauseating effects (pica behavior). Surprisingly, ICV relaxin-3 did not attenuate central GDF-15 induced anorexia, nausea and body weight reducing effects. Lastly, ICV relaxin-3 did not attenuate the anorexic and nauseating effects of systemic LiCl administration. These data suggest that central relaxin-3 attenuates the anorectic and body weight reducing effects of systemic cisplatin, but not its nauseating effects, through potentially a GDF-15 independent pathway; offering a new therapeutic target to be combined with the polypharmacy approach of treating chemotherapy-induced side effects.

P157 **The Effect Of Vertical Sleeve Gastrectomy On The Regulation Of Food Intake By Agrp Neurons**

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Vertical sleeve gastrectomy (VSG) is an effective obesity treatment that decreases food intake and produces long-term weight loss and metabolic improvements. We investigated whether reduced feeding after VSG could be explained by changes in the regulation of feeding by Agouti-Related Peptide (AgRP) neurons in the hypothalamic arcuate nucleus (Arc).

For all experiments, we used male AgRP-Cre mice maintained on a high-fat diet for 8-12 weeks prior to VSG or a sham surgery. First, we used chemogenetics to selectively drive the activity of Arc AgRP neurons in VSG (n=7) and sham (n=7) mice. Chemogenetic activation of these neurons increased consumption of various foods, including standard rodent chow, high-fat chow, a 10% sucrose solution, and a lipid emulsion. Notably, stimulating Arc AgRP neurons increased feeding to the same degree in *both* VSG and sham animals, demonstrating that reduced feeding after VSG is *not* due to physical restriction on the amount of food that can be consumed. To examine whether VSG alters the basal activity of these neurons during feeding, we next conducted *in vivo* fibre photometry recordings as a proxy for Arc AgRP neuronal activity in a separate cohort of mice. Animals were food-deprived overnight then presented with a pellet of high-fat chow during photometry recordings. Analysis of photometry signals pre- and post-consumption indicated that VSG mice (n=7) show greater suppression of bulk Arc AgRP neuronal activity upon feeding compared with *ad libitum* fed (n=6), but not weight-matched (n=7), sham mice. Together, our findings demonstrate that VSG does not disrupt AgRP-mediated feeding, and indicate that VSG may restore the normal functioning of Arc AgRP neurons in response to feeding.

P159 **A Sensometric Study Of Chocolate Preference Combining Neuroimaging And Olfactometry**

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Rationale: To explore the complexity underlying food preferences, this study examined links between neural and sensory attributes with chocolate preference. Hypothesis: Prefrontal cortex (PFC) activity will differ between chocolate likers (CL) and neutral/dislikers (ND) during exposure to chocolate aroma vs. neutral air. Species: Human participants, aged 18-45 years. Number of subjects: Ten participants (3 males, 7 females) in this preliminary analysis. Procedures: Participants self-reported chocolate preference on a 9-point Likert scale, and their height (m) and weight (kg) were measured to calculate body mass index (BMI). A functional near-infrared spectroscopy (fNIRS) cap measured PFC activity during the experiment (22 channels). Chocolate aroma or neutral air was presented in a pseudorandomized fashion using an olfactometer. Instructions for “smell” (10 seconds) and “rest” (15 seconds) periods were displayed on a screen, totaling to 32 “smell” periods: 16 chocolate and 16 neutral air. General linear models analyzed oxyhemoglobin (HbO) response in each fNIRS channel for the neutral air and chocolate aroma conditions. The beta coefficients obtained represented the amplitude of the changes in each experimental condition for every participant. These coefficients were used in a 2 (aroma condition: chocolate vs. neutral air) x 2 (chocolate preference: CL vs. ND) mixed-design analysis of variance adjusted for BMI. Results: HbO was significantly lower in 1 channel in the left orbitofrontal area during chocolate aroma exposure compared to neutral air ($p=0.04$, $n=10$). CL (n=7) had significantly lower HbO in 6 channels in the orbitofrontal and dorsolateral PFC areas on average during the experiment compared to ND (all $p<0.05$). No significant interaction was present between aroma condition and preference group. Relevance: Research that combines neuroimaging and olfactometry may help uncover neural signatures for food preferences.

P161 **Brainstem Prrp And Ppg Projections To The Dorsomedial Hypothalamus Reduce Food Intake Without Reducing The Activity Of &Ldquo;Hunger&Rdquo; Neurons**

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Anorectic signals from the gut reach the brain via the brainstem nucleus of the tractus solitarius (NTS). Two phenotypically-defined anorectic neuron populations within the NTS contain either prolactin-releasing peptide (PrRP) or preproglucagon (PPG). While $PrRP^{NTS}$ neurons are responsive primarily to meal-related satiety signals, PPG^{NTS} neurons respond to more aversive stimuli. Both neurons induce anorexia when stimulated and, thus, may converge on common downstream targets. Hunger-promoting agouti-related peptide neurons in the hypothalamic arcuate nucleus ($AgRP^{ARC}$) are inhibited by a variety of anorectic stimuli. The central pathways leading to $AgRP^{ARC}$ inhibition are yet to be fully defined, but potential relays in the NTS and dorsomedial hypothalamus (DMH) have been implied. Using a combination of chemo- and optogenetics, we have identified central pathways utilised by $PrRP^{NTS}$ and PPG^{NTS} neurons, including direct projections from the NTS to the DMH. Selective activation of either population, using Cre-dependent stimulatory designer receptors, reduces both normal night-time feeding and fast-induced refeeding, as well as inducing cFos in the DMH and other potential downstream targets. To demonstrate these projections are sufficient to reduce feeding, we used Cre-dependent optogenetics to activate terminals in the DMH. Selective optogenetic stimulation of $PrRP^{NTS \rightarrow DMH}$ or $PPG^{NTS \rightarrow DMH}$ projections reduced feeding in hungry mice. Finally, by combining chemogenetics and fibre photometry, we demonstrated that stimulation of $PrRP^{NTS}$ or PPG^{NTS} neurons reduced food intake without inhibiting the activity of $AgRP^{ARC}$ cells. In summary, these two NTS→DMH projections represent parallel pathways that can cause anorexia without necessarily switching off hunger.

P163 **An Incretin Dependent Periprandial Population Of Neutrophils In Blood Patrols The Metabolic Adaptations To High Fat Diet**

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Today we mostly live in “periprandial” state, consuming abundant amounts of high fat diets (HFD) over most of the day. HFD alters the fine tuning of Glucagon Like Peptide-1 (GLP-1) and insulin dependent metabolic adaptations, and it expands the innate arm in bone marrow (BM). We hypothesize that innate immune cells promptly patrol the circulation in response to GLP-1 signal against the adverse metabolic adaptations to HFD. To test if innate immune cells populate the circulation during HFD, we immunophenotyped the blood of mice fed seven days either HFD (60% energy from fats) or standard fat diet (herein, “SFD”), both in periprandial state and over 4 hours HFD or SFD refeeding following an overnight fasting. We studied if GLP-1 signaling and its insulinotropic effect impact this phenomenon. Neutrophils rapidly populate the blood during HFD refeeding only, independent from BM pool. The periprandial increase of blood neutrophils was attenuated upon i.p. injection of exenamide3-39, a GLP-1 receptor antagonist (15 minutes before refeeding); Concomitant insulin i.p. injection restored the periprandial increase of neutrophils blood count. During this phenomenon, the plasma concentrations of neutrophil-specific “call-me” proteins rapidly increase, before the GLP-1 dependent periprandial alterations. We

recapitulated this observation also in immunodeficient RAG2KO/IL2rg-KO/CD47-KO mice, which lack the lymphoid arm. Finally, we clinically translated a higher periprandial increase of neutrophils blood count in >24,000 individuals affected by type 2 diabetes from UK-Biobank cohort. We propose an incretin-dependent periprandial mechanism that impacts an innate phenomenon, to probably alert the body to the inflammatory consequences of metabolic alterations.

P165 **Impact Of Dietary Carbohydrates On Glucagon-Like Peptide-1 Agonist-Induced Weight Loss Via Fgf21 Signaling**

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Glucagon-like peptide-1 receptor (Glp1R) agonists (Glp1RA) promote a wide range of weight loss. We show that dietary carbohydrate (carb) content influences Glp1RA-induced weight loss via a Fibroblast Growth Factor-21 (FGF21) mechanism: 1) Glp1RA increase plasma FGF21 via neuronal Glp1R, 2) the Glp1RA liraglutide (lira) promotes more weight loss in starch-based high vs. low carb-fed mice, and 3) this effect is lost in liver FGF21 knockout (LKO) mice and mice lacking neuronal b-Klotho (Klb), the FGF21 co-receptor. We hypothesize that lira targets proopiomelanocortin (POMC) Glp1R to increase FGF21, and FGF21 targets ventromedial hypothalamus (VMH) Klb to reduce weight in high carb-fed mice. We measured plasma FGF21 levels in fasted control and POMC Glp1r knockout mice prior to and 7h post injection with vehicle or lira. High carb-fed VMH Klb knockout and control mice were treated with vehicle or lira for 14d with daily weight readings. We also hypothesize that lira promotes more weight loss in mice fed a high sucrose diet and this is attenuated in LKO mice. Control and LKO mice were fed low vs. high sucrose diets for 12 wks and were treated with vehicle or lira for 14d with daily weight readings. Lira increased FGF21 in control ($p<0.01$) but not POMC Glp1r knockout mice (n=7-9/group). Lira reduced weight equally in control and VMH Klb knockout mice (n=12/group) suggesting that other brain regions mediate the effect of lira-induced FGF21 on weight loss. Lira reduced weight equally in control and LKO mice fed low vs. high sucrose diets (n=8-10/group), suggesting that lira-induced FGF21 affects body weight in starch but not sucrose-fed mice. Future studies will further investigate mechanisms by which carb content influences Glp1RA-induced weight loss.

P167 **Predictors For Fasting Plasma Erythritol Concentrations In Different Populations**

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Introduction: The sugar alcohol erythritol is popular for its non-caloric, low-glycemic, low-insulinemic, and satiating properties. Erythritol occurs naturally but is also endogenously produced via the pentose-phosphate pathway. Untargeted metabolomic studies have linked increased plasma erythritol concentrations with metabolic disorders like diabetes. Weight loss was associated with decreased plasma erythritol concentrations along with a reduction in insulin resistance. This study aimed to identify predictors of fasting plasma erythritol concentrations in different populations. **Methods:** In this retrospective study, fasting plasma samples from 218 participants were analyzed: 50 adults and 30 adolescents with normal weight, and 138 adults with obesity, 15 of whom had undergone bariatric surgery. Except for patients who had undergone bariatric surgery, regular erythritol consumption was an exclusion criterion for all other participants. Fasting plasma erythritol, glucose, and insulin concentrations were measured, and their effects on fasting erythritol were assessed using linear regression models. **Results:** Across all populations, age ($\beta=0.14$, SE=0.03, $p<0.01$) was a significant predictor of fasting erythritol concentrations, while BMI, sex, fasting glucose, and insulin were not: a higher age was associated with higher erythritol concentrations. After bariatric surgery, ΔBMI ($\beta=0.34$, SE=0.16, $p=0.04$) predicted Δerythritol, with a decreased BMI associated with decreased fasting erythritol concentrations. **Conclusions:** We identified age and change in BMI but not fasting glucose or insulin as predictors for fasting plasma erythritol concentrations. These findings indicate that increased plasma erythritol concentrations might be the consequence and not course of metabolic disorders.

P169 **Dietary Protein Restriction Increases Operant Responding To Msg In An Fgf21-Dependent Manner**

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Umami taste is inherently associated with protein-rich foods that contain glutamate and nucleotides such as IMP and GMP, but not with pure carbohydrates or fats. Therefore, umami is thought to serve as a cue for the presence of protein. Our previous study showed that mice on a protein-restricted diet develop an increased motivation for protein, and that this nutrient-specific preference requires FGF21 signaling. We hypothesized that monosodium glutamate (MSG), which is typically only weakly attractive when presented alone, becomes highly preferred under protein restriction, and that FGF21 signaling is necessary for this preference to develop. Male wild-type and FGF21 knockout (FGF21-KO) mice were fed either a control or low-protein (LP) diet for 7–10 days, and the following studies were conducted: (1) MSG and water consumption were measured over 3 days; (2) mice were trained to nose poke for either MSG or water across a series of increasing fixed ratio values; (3) the activity of VTA dopaminergic neurons was assessed following intraoral delivery of either MSG or water using*Th*-Cre or *Th*-Cre;*Fgf21*-KO mice. Data were analyzed using SAS version 10 (SAS Institute) via one-way or two-way ANOVA. Mice on the LP diet showed increased consumption of MSG and enhanced operant responding for MSG compared to controls. They also exhibited slightly elevated dopaminergic neuron activity in response to MSG versus water. These LP diet effects were abolished in FGF21-KO mice. A previous study demonstrated that umami preference in mice can be influenced by prior taste experiences. Our findings suggest that an animal's internal protein status also modulates preference for umami solutions, and that FGF21 signaling is essential for the development of this protein restirction-driven umami preference.

P171 **Influence Of Mid-Morning Snack Size On Satiety And Emotions**

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The objective of this study was to investigate the emotions associated with different satiation and satiety states. For this, fifty participants (21 to 49 years; 68% were female and 32% male) attended six separate sessions: two sessions with

their usual food and amount; two sessions in which 50% more of the amount was added; and two sessions in which 50% of the amount was taken away. Satiation level after the intake and satiety/hunger at two hours were recorded for each session, as well as the emotional response (adapted version of EsSense Profile). Each participant selected and described the midmorning snack (food type and quantity) in a previous individual session. The order of the sessions was varied among participants following a balanced design. For each evaluation condition (normal, 50% more or 50% less food), the satiety and hunger were studied through one -way ANOVA. In each condition it was possible to expose around 70-80% of panelists to the desired level of satiety. However, there were cases (approx. 30%) where there was not a complete match between quantity and satiety. For each condition, correspondence analysis was conducted with the frequency values of the selected emotions in each situation. The emotions unsatisfied, good, disappointed, tired, typical of those who become under-satiated. The emotional profile when satiated and very satiated are similar, although there are differences. In the case of the very satiated, they felt fuller, satisfied, happy, and joyful, whereas when they were satiated, the terms: pleased, calm were more prominent. It would be ideal to adjust diets to the amount to reach the right point of satiety while generating positive emotions.

P173 **Cafeteria Diet Exposure, And Not Weight Gain Propensity, Impacts Gut Microbiota Of Rats &Ndash; A Within Laboratory Meta-Analysis**

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While differences in gut microbiota diversity and composition are seen in animal models of obesity, whether there are differences between obese-prone and obese-resistant subjects is unknown. We addressed this question in an internal meta-analysis testing whether diet-induced gut microbiota changes are related to individual differences in obesity proneness, defined by diet-induced weight gain in response to high-fat, high-sugar 'cafeteria' diet. Methods: Using faecal microbiome data from our validated model of diet-induced obesity (12 studies, 208 male and 74 female Sprague-Dawley rats, exposed to 3.5-13 weeks of healthy (chow) or cafeteria diet), we determined whether gut microbiota alpha diversity and composition differed between obese-prone and obese-resistant rats (top & bottom tertiles, based on percentage weight gain; Wilcoxon t-test). Results: We found consistent effects of cafeteria diet on the gut microbiota, with marked changes in overall composition, and reduced gut microbial richness (95% CI: -0.24, -0.01, $t(11)=2.441$, $p=0.0328$), Shannon's diversity index (95% CI: -0.06, -0.01, $t(11)=3.006$, $p=0.0119$) and gut microbial evenness (95% CI: -0.02, -0.01, $t(11)=4.961$, $p=0.0004$) relative to control. Specific microbial genera previously associated with obesity, such as *Bacteroides* and *Blautia*, were enriched by cafeteria diet. Critically, alpha diversity measures and gut microbiota composition did not differ between obese-prone and obese-resistant rats in either diet group. Conclusions: Microbiota composition is substantially altered by cafeteria diet, but these changes appear unrelated to resultant weight gain. Our work suggests interventions solely targeting the gut microbiota are unlikely to result in meaningful reductions in diet-induced weight gain or adiposity.

P175 **Drinking Microstructure Analysis Of Direct Controls Of Water Intake In Male And Female Rats.**

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Measures of rodent licking patterns are used to test how various manipulations affect fluid intake. Decades of research indicates that manipulating satiation affects the number of licking bursts whereas manipulating the hedonic value of the solution affects the size of the licking bursts. This type of analysis has been largely applied to things that modulate drinking (i.e., indirect effects), but it is unclear if it is appropriate to use for a primary (direct) control of intake. Furthermore, it remains unclear which of the licking parameters (if either) vary as a function of the strength (dose) of the primary dipsogen. A better understanding of this could provide insight into how drinking is stimulated. Accordingly, we performed three experiments to examine lick patterns after varying doses of angiotensin II (0-100 ng), carbochol (0-100 ng), and hypertonic saline (0.15-2 M) in male and female rats (n = 12-14 per experiment). As expected, AngII dose-dependently increased licks for water ($p < 0.001$), an effect that was greater in males than in estrus females ($p < 0.05$). Similar dose-related increases in burst number ($p < 0.001$), but not burst size, were observed. Hypertonic saline dose-dependently increased licks for water ($p < 0.001$) which was associated with an increase in burst number ($p < 0.001$) but not burst size. Preliminary data suggests that carbochol dose-dependently increases licks for water, which also appeared to be associated with an increase in burst number but not burst size. Together, this suggests that increasing the strength of the direct control of water intake affects burst number, without a dose-related changes in burst size. This suggests that stimulating water intake is the result of decreasing or overriding satiety signals.

P177 **Effects Of Obesity On Liver Gaba Shunt Flux.**

Anisha Venigalla[1], Kayla Mac[1], MariKate Murphy[1], Maya Paley[1], Jonathan Valeros[2], Jessica B. Spinelli[2], Benjamin J. Renquist[1]

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Rationale: The GABA shunt is classically thought of as a GABA disposal pathway that is highly active in the CNS and liver and is dependent on 2 enzymes, GABA transaminase and succinate semialdehyde dehydrogenase. We previously showed

that liver lipid accumulation results in liver GABA production dependent on the GABA shunt. This liver produced GABA increases phagic drive and causes insulin resistance and hyperinsulinemia. Hypothesis: Obesity results in reversal of the canonical direction of GABA shunt from GABA breakdown to GABA production. Species, Subjects, and Procedures: We assigned 12-week old adult male C57Bl/6J mice to chow or high fat diet (60% of calories from fat, Td.06414, Envigo; n = 5). After 10 weeks of diet treatment, we injected L-Glutamine ($^{13}C_5$, $^{15}N_2$) intraperitoneally (75 mg/kg) and 30 minutes later sacrificed the mice, collected, and snap froze the liver for analysis by liquid chromatography-mass spectrometry. Data was analyzed by t-test with Bonferroni correction for multiple comparisons. Results: Obesity increased liver concentrations of both $^{13}C_4$ labelled and unlabeled succinate, succinate semialdehyde, and GABA ($P = 0.0491$, $P = 0.0637$, $P = 0.0047$). Obesity had no effect on liver fumarate concentration. This helps to establish the key role of succinate dehydrogenase (complex II) in obesity induced dysregulation of the TCA cycle. GABA was not ^{15}N labeled, supporting that GABA production was independent of glutamate decarboxylase. Conclusions: This data establishes that diet induced obesity increases GABA shunt flux toward GABA production. These findings provide support for further investigation of liver GABA shunt activity in obesity and the resulting physiological consequences.

P179 **Development Of A College Course Focused On Human Weight Regulation And Lesser-Known Contributors To Increased Adiposity/Obesity**

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Introduction: “What causes obesity?” The typical response is usually “eating too much and not exercising enough.” Few people are aware of the complexity of body weight regulation, which can lead to weight bias. **Objective**: Here, I describe an 8-week, 2-credit course entitled “Physiology of Weight Regulation,” which was developed for undergraduate students to introduce them to how body weight is regulated. Emphasis is placed on genetic, physiological, and environmental contributors to adiposity. The course was first offered at the College of Saint Benedict and Saint John’s University (Minnesota, USA) in the spring of 2013, and has been taught a total of 12 times. **Course Format**: The course is a blend of lecture and discussion. Prior to covering a topic, students are assigned a reading (journal article or book chapter). As they read, students utilize the Purposeful Reading method, which entails: 1) Writing down four significant concepts encountered in the article; 2) Listing two facets of the article that were difficult to understand; and 3) Listing one question they would ask the author of the article if given the chance. At the start of each class, students are divided into groups to discuss their Purposeful Reading write-ups. The instructor then opens the discussion to the entire class. A lecture on the topic follows. Eighteen topics are covered in the course, e.g., The Central Nervous System Regulation of Food Intake and The Gut Microbiome & Body Weight. **Conclusions**: Student feedback from course evaluations available for seven sections (49 students reporting) show that 100% of students found the *course as a whole* to be excellent, very good, or good, and 96.9% found the *course content* to be excellent, very good, or good.

P181 **Dorsal Hippocampus Food-Responsive Neurons Promote Location Memory**

Nicolas Morano, Lea Decarie-Spain, Logan Lauer, Cindy Gu, Scott Kanoski
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The hippocampus (HPC) is a critical regulator of mnemonic processes and food intake control. Our recent work identified a population of ventral HPC (vHPC) neurons that is recruited during food consumption to selectively encode spatiotemporal information surrounding a meal. Whether the dorsal HPC subregion (dHPC) contains neurons with similar capabilities is unknown. Following a 24h fast, rats were given free access to standard laboratory chow for 30min during which bulk dHPC calcium-dependent activity was recorded. Results showed increased activity during eating bouts, suggesting that dHPC neurons are recruited during active food consumption. To verify the functional role of these dHPC food-responsive neurons, we employed a targeted recombination in active populations viral approach. Rats received injections of a tamoxifen-inducible virus in the dHPC expressing Cre-recombinase driven by a Fos promoter, paired with a Cre-dependent virus expressing diphteria toxin fragment A (dTA) to ablate the meal-activated neurons. Recombination with tamoxifen was induced after rats were fasted for 24 hours and either given no food (‘Fasted’) or a 30-minute meal (‘Fed’). While ablation of dHPC food-responsive neurons had no effect on weight regulation, performance in a meal place recognition task was impaired in ‘Fed’ rats. To evaluate if these neurons only promote food-related location memory, the same cohort was assessed in the novel object location recognition task. Similarly, performance was impaired in rats with ablated dHPC food-responsive neurons, indicating generalized location memory deficits. Together, these results characterize a population of dHPC neurons engaged by eating that, unlike vHPC neurons, function to encode both meal-dependent and meal-independent spatial memory.

10:00 - 12:00 PM	L1
Presidential Symposium	

Chair(s): Mitch Roitman

10:00 **A Gut (Microbiome) Feeling: Brain Body Interactions Regulating Behaviour Across The Lifespan**
John Cryan
University College Cork, Cork, Ireland

The prevalence of brain disorders, including stress-related neuropsychiatric disorders and conditions with cognitive dysfunction, is rising. Poor dietary habits contribute substantially to this accelerating trend. Recently, the communication between the microorganisms within the gastrointestinal tract and the brain along the gut–brain axis has gained prominence as a potential tractable target to modulate brain health. The microbiota and the brain communicate with each other via various routes including the immune system, tryptophan metabolism, the vagus nerve and the enteric nervous system, involving microbial metabolites such as short-chain fatty acids, branched chain amino acids, and peptidoglycans. Many factors can influence microbiota composition in early life, including infection, mode of birth delivery, use of antibiotic medications, the nature of nutritional provision, environmental stressors, and host genetics. At the other extreme of life, microbial diversity diminishes with aging. Stress, in particular, can significantly impact the microbiota-gut-brain axis at all stages of life. Animal models have been paramount in linking the regulation of fundamental neural processes, such as neurogenesis and myelination, to microbiome activation of microglia. Moreover, translational human studies are ongoing and will greatly enhance the field. Future studies will focus on understanding the mechanisms underlying the microbiota-gut-brain axis and attempt to elucidate microbial-based interventions for neuropsychiatric disorders. The composition and function of the gut microbiota is robustly influenced by dietary factors to alter gut–brain signalling. To reflect this we recently proposed that a diet–microbiota–gut–brain axis exists that underpins health and well-being.

10:30 **From Nutrients To Neurons In The Gourmet Fly: How Brain-Body Interactions Guide Dietary Decisions**
Carlos Ribeiro
Champalimaud Foundation, Lisboa, Portugal

A balanced intake of different classes of nutrients is a key determinant of health, wellbeing, and aging. To ensure nutrient homeostasis animals adapt their foraging strategies according to their current and future needs. We want to understand how animals decide what to eat, how these decisions are shaped by brain-body interactions, and how these decisions affect the fitness of the animal. To achieve a mechanistic, integrated, whole-animal understanding of nutritional decision-making we work at the interface of behavior, metabolism, microbiome, and physiology in the adult Drosophila melanogaster. I will discuss how the powerful combination of activity imaging approaches, neurogenetics, connectomics, automated, quantitative behavioral analyses, and nutritional and microbial manipulations is allowing us to achieve a mechanistic understanding of how internal states shape neuronal circuits to optimize complex foraging decisions.

11:00 **Food For Thought: Behavioral And Brain Characterization Of Anxiety-To-Eat In Anorexia Nervosa**
Kimberly R. Smith
Department of Psychiatry and Behavioral Sciences, Johns Hopkins School of Medicine, Baltimore, MD, United States

Homeostatic and non-homeostatic signals that control ingestive behaviors are often overridden by maladaptive eating behaviors (e.g., food avoidance) to achieve a low body weight in anorexia nervosa (AN). Recently our lab has been interested in characterizing anxiety-to-eat experienced by individuals with AN, with the overarching hypothesis that anxiety-to-eat underlies the severe food avoidance and restrictive eating behaviors that contribute to poor health and treatment outcomes for AN. The present work will focus on our investigations to 1) behaviorally characterize anxiety-to-eat in AN and in healthy individuals, 2) determine the neural correlates of anxiety-to-eat using functional magnetic resonance imaging, 3) identify the neurobiological mechanisms underlying anxiety-to-eat using magnetic resonance spectroscopy, and 4) determine the extent to which anxiety-to-eat improves with behavioral inpatient treatment that includes a meal-based nutritional protocol to achieve rapid weight restoration. Our data suggest that anxiety-to-eat contributes to maladaptive eating behaviors, involves a distributed network of brain regions with a potential therapeutic target, and is treatable with nutritional rehabilitation focused on rapid weight gain and a broadened food repertoire.

11:30 **Social Influences On Eating**
Suzanne Higgs
School of Psychology, University of Birmingham, Birmingham, United Kingdom

What and how much people eat is influenced by the social context of consumption. For example, people tend to adapt their food choices to those of others, which is known as modelling and they also use their eating behaviours to convey a favourable impression of themselves to other people, which is known as impression management. One particularly striking effect is that people tend to eat more when dining with familiar company compared to eating alone, a phenomenon known as the social facilitation of eating. This presentation will explore recent research on how social factors shape eating behaviours, with a particular focus on social facilitation. I will highlight key gaps in our understanding and suggest promising directions for future research. Gaining deeper insights into the impact of social context on eating choices could lead to new strategies for encouraging healthier eating habits.

12:10 - 1:40 PM	L1
Oral Session 1: All the feels; interactions between stress, emotion and ingestion	

Chair(s): Eric Krause

12:10 **An Influence Of Bmi And High Fat Diet On Food Valuation**

Justin Sung[1], Filip Morys[1], Antonietta Canna[1], Xue Davis[2], Dana M Small[1, 2]

[1]McGIll University, Montreal, QC, Canada, [2]Yale University, New Haven, CT, United States

In individuals with healthy weight (HW), implicit versus explicit nutritional signals are relatively more important in determining food value. For example, in auction tasks, willingness to pay (WTP) is positively associated with actual but not estimated energy density and people will pay more for equally pleasant, familiar, priced and caloric foods composed of carbohydrate and fat (COMBO) compared to primarily carbohydrate (CARB) or fat (FAT) alone (Tang 2014; DeFeliceantonio 2018; Perszyk 2021). Unexpectedly, the opposite appears to be true in individuals with overweight or obesity (OW/OB) where WTP is inversely related to actual energy density – an effect mediated by food price (Perszyk 2021). Here, we used an auction task to investigate factors driving WTP in a sample of 51 participants with OW/OB enrolled in a weight loss trial. Consistent with previous findings, a negative association was observed between WTP and actual energy density that was mediated by food price ($p=0.02$). We also observed an effect of macronutrient in which participants bid more for FAT than CARB ($p=0.003$), with the magnitude of the effect increasing as BMI increased ($p=0.01$). Notably, these effects were independent of liking and portion size, which were independent predictors of WTP ($p<0.001$ and $p = 0.02$, respectively). Self-reported intake of saturated fat was positively associated with WTP in all macronutrient categories ($p=0.007$). These results (1) provide further support that price is a greater influence on food choice than is energy density in individuals with OW/OB; (2) reveal a novel association between high fat diet and increased food valuation for all macronutrient categories; and (3) demonstrate a bias for FAT versus CARB foods as a function of increasing BMI.

12:25 **Not Only Gut Feelings: Pancreatic Hormone, Amylin, Controls Emotionality And Sociability, In A Sex Divergent Manner.**

Suyeun Byun[1,2], Morgan R Sotzen[1,2], Doris I Olekanma[1,2], Mya A Knappenberger[1,2], Karolina P Skibicka[1,2]

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Amylin, a pancreatic peptide hormone, has gained attention for its role in appetite regulation and potential as an anti-obesity treatment; however, its effects on emotionality remain largely unexplored. Given that feeding-related peptides often influence metabolic, but also psychiatric functions, via overlapping neural circuits, we investigated the role of amylin in modulating different aspects of emotionality and sociability: anxiety, depression, aggression, and social behavior. We hypothesized that amylin administration influences emotional behaviors in a sex-specific manner, with the central amygdala (CeA) as a critical site mediating these effects. The CeA was selected as we recently found this nucleus is critical for amylin's feeding behavior control, and it is a brain site well recognized for its important role in emotionality and sociability control. Male (n=11-14) and female (n=12-19) Sprague-Dawley rats received either systemic (500 µg/kg, IP) or intra-CeA (0.1 or 0.4 µg) amylin. Behavioral assessments included the elevated plus maze (EPM), acoustic startle response (ASR), forced swim test (FST), resident-intruder test (RIT), and social interaction test (SIT), with data analyzed using t-tests or ANOVA with post-hoc Holm-Sidak tests ($p<0.05$). Systemic and CeA amylin administration induced sex-specific effects on anxiety-like behavior, with anxiolytic responses in males and anxiogenic responses in females. Intra-CeA amylin increased depressive-like behavior in females but had no effect in males. Aggressive behavior was reduced in both sexes, while systemic, but not intra-CeA, amylin increased social interaction. These findings suggest that amylin modulates emotional and social behaviors in a sex-dependent manner, with the CeA as a key neural substrate. Considering previous anti-obesity therapeutics have been withdrawn from the market because of emotionality side effects, our results highlight the importance of understanding these effects in both sexes for the development of safe amylin-based obesity treatments that minimize psychiatric risks.

12:40 **Stress Engages The Noradrenergic Brainstem-To-Hypothalamus Circuit To Suppress Appetite.**

Myungmo An[1,2], Junkoo Park[1,2], Sumin Lee[3,4], Se-Young Choi[3,4], Sung-Yon Kim[1,2]

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Stress triggers adaptive behavioral shifts that override homeostatic drives such as appetite, yet the underlying neural mechanisms remain poorly understood. Here, we identify a noradrenergic brainstem-to-hypothalamus circuit that mediates stress-induced appetite suppression in mice. Using *in vivo* fiber photometry, we found that noradrenergic locus coeruleus (LC^{NA}) neurons exhibit persistent activity extending beyond acute restraint stress, temporally aligned with feeding suppression (n=7). Inhibition of LC^{NA} neurons (n=11) or their projections to the paraventricular hypothalamus (PVH) (n=19) prevents stress-induced appetite suppression, whereas optogenetic activation of LC^{NA} neurons mimics stress effects that suppress feeding (n=7). Real-time norepinephrine recordings in the PVH show sustained elevation after restraint stress, correlating with the duration of feeding suppression (n=8). Pharmacological blockade of α1-adrenergic receptors in the PVH, particularly the α1b subtype, abolishes stress-induced appetite suppression (n=9). Notably, this circuit is also required for feeding suppression after chronic stress (n=5). Collectively, our findings pinpoint the LC^{NA}-$PVH^{\alpha 1b}$ noradrenergic circuit as a key driver of sustained appetite suppression following stress, uncovering a direct link between brain stem arousal center and hypothalamic feeding circuits.

12:55 **The Role Of The Basolateral Amygdala And The Lateral Hypothalamus In Social Stress-Induced Appetitive Motivation**

Megan L. Mcgraw, Cooper C. Christensen, Ai-Jun Li, Emily Qualls-Creekmore
Washington State University, Pullman, WA, United States

Stress profoundly influences appetitive motivation. While stress can promote maladaptive behaviors such as behavioral addictions or contribute to disorders like depression, the underlying neural mechanisms remain unclear. The basolateral amygdala (BLA) and lateral hypothalamus (LH) are key regulators of both stress and motivated behaviors, yet their direct interactions remain underexplored, particularly across sexes. Our recent findings reveal that chronic non-discriminatory social defeat stress (CNSDS) elicits opposite effects on appetitive behavior in male and female mice. We hypothesize that BLA glutamatergic projections to the LH (BLA^{Glut}→LH) mediate these sex-specific effects. To test this hypothesis, we measured neural activity in response to CNSDS and tested the effect of circuit manipulation on appetitive motivated behavior. All experiments were conducted in male and female C57BL/6J or Vglut2-ires-cre mice, n = 5-7 per group. First, we confirmed direct monosynaptic BLA^{Glut}→LH connectivity using cell-type specific viral tracing. Next, we found that cFos expression after CNSDS was increased in the BLA and LH of both sexes. Fiber photometry also revealed that calcium dynamics in BLA^{Glut} terminals in the LH are increased during CNSDS in both sexes. Finally, optogenetic excitation of the BLA^{Glut}→LH circuit enhances motivated behavior in non-stressed mice of both sexes. Given the established sex differences in BLA physiology, and heterogenous molecular and functional profile of BLA neurons, we propose that CNSDS engages different BLA subpopulations in males and females that translate into opposing outcomes on motivation. These findings highlight the need for sex-inclusive neurobiological research and may inform targeted interventions for stress-related disorders.

1:10 **Functional Neuroimaging Of Impulsivity, Negative Emotional Reactivity And Monetary Reward Processing In Adults With Obesity And Binge Eating Symptoms**

Alisa Musatova[1], Navpreet Chhina[1], Rioghnach Hannan[1], Eleanor Brian[1], Moaz Al Lababidi[1], Ghadah Aldubaikhi[1], Isabelle Franco[1], Madhawi Aldhwayan[2], Werd Al-Najim[3], Aruchuna Ruban[4], Michael A Glaysher[5], Christina G Prechtl[6], James P Byrne[5], Julian P Teare[4], Anthony P Goldstone[1]

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Introduction: Binge eating symptoms (BES) may be associated with impulsivity and emotional regulation difficulties (risk factors for disordered eating, with binge episodes often precipitated by stress) and abnormal reward processing. The neural correlates of these facets in BES are uncertain. **Methods:** N=96 adults with obesity ± type 2 diabetes mellitus with (≥ 1 episode/mo) or without BES (BMI/sex-matched) completed questionnaires, and n=44 non-food Go/No-Go (GNG), negative emotional reactivity (NERT), monetary incentive delay (MID) fMRI tasks after an overnight fast. ROI/whole-brain analyses examined BOLD signal during successful motor response inhibition (GNG), unpleasant (vs. neutral) image viewing (NERT), win/loss vs. neutral trial anticipation (MID) ± plasma glucose/BMI as covariates. **Results:** In BES vs. non-BES there was: (i) in GNG task, more commission errors, and during successful No-Go trials lower BOLD signal in precentral gyrus (pCG), operculum, posterior cingulate gyrus, precuneus, lat. occipital cortex, higher BOLD signal in mid./sup. frontal gyrus, pCG; (ii) higher trait impulsivity from negative/positive urgency (UPPS-P), but not monetary temporal impulsivity (delay discounting), (iii) worse mood (HADS, BDI-II), quality-of-life (IWQoL-Lite, SF36); (iv) in NERT, lower BOLD signal to unpleasant images in amygdala (negatively correlating with impaired QoL), subcallosal cortex, lingual gyrus; (v) similar BOLD signal during monetary reward anticipation. **Conclusion:** Monetary reward processing was unaffected by BES. Heightened urgency and impaired motor response inhibition are consistent with greater impulsivity in BES. Attenuated negative emotional reactivity in amygdala and subcallosal cortex in BES may indicate habituation to chronic stress.

1:25 **Gip Receptor Agonism Modulates Aversive Behaviors And Parabrachial Cgrp Neuron Activity (New Investigator Travel Awardee)**

Haley Province[1], Nathan Leong[1], Jessica Xia[1], Nikolas Hayes[1], Lisa Beutler[1]

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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. Pharmacologic activation of the GIPR modestly suppresses feeding, and the recently developed obesity and diabetes therapy tirzepatide acts in part as a GIPR agonist. Recent reports have also demonstrated that central GIP receptor agonism may also be anti-aversive. Data from multiple species have shown that GIPR agonism markedly attenuates nausea and vomiting in response 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 without reducing its anorexigenic effects in mice. 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 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. Moreover, our data supports recent studies that anorexia and aversion are regulated by distinct neural pathways.

12:25 - 1:40 PM	L2
Oral Session 2: Coming to your senses; olfaction and gustation in ingestion	

Chair(s): Ann-Marie Torregosa

12:25 **High Or Low Dietary Sweet Taste Exposure Do Not Affect Sweet Taste Liking Or Body Weight**

Eva Cad[1], Monica Mars[1], Leone Pretorius[2], Claudia Tang[2], Merel van der Kruijssen[1], Hanne de Jong[1], Michiel Balvers[1], Katherine Appleton[2], Kees de Graaf[1]

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Rationale: Humans love sweet taste, but our innate liking may result in excessive consumption, high energy intake and overweight. Authoritative public health agencies follow the reasoning: more frequent exposure to sweet taste increases preferences for sweetness, which leads to greater sugar and calorie intake and, eventually, leads to higher body weight. However, none of these steps have been confirmed with experimental data. **Hypothesis:** There will be no effects of high or low dietary sweet taste exposure on sweet taste liking, energy intake or body weight. **Species:** Human adults **Number of subjects:** 180 **Procedures:** A large-scale 6-month, randomized clinical trial (registration: clinicaltrials.gov NCT04497974: Sweet Tooth: Nature or Nurture?) was undertaken with three experimental groups: higher, regular and lower dietary sweetness exposure. Ad-libitum diets with partial food provision were designed as equicaloric. Outcomes were sweet taste liking, sweet taste perception, energy intake, body weight and several biomarkers for diabetes and cardiovascular disease. **Results:** A higher/lower dietary exposure to sweet taste did not lead to higher/lower sweet taste liking, changes in perception, energy intakes, body weight or biomarkers for diabetes and cardiovascular disease. Subjects also spontaneously returned to baseline levels of sweet food intake at 1 and 4 months follow up. **Conclusions:** Our findings directly contradict the assumptions made by many public health agencies, and suggest that, while overweight remains a global public health concern, excess energy intake is unlikely to be affected by advice to reduce our exposure to, or intakes of, sweet taste. Dietary recommendations to avoid energy overconsumption should instead focus on effective evidence-based strategies.

12:40 **Olfactory Bulb Glp-1 System Influences Sensory Perception Of Food And Feeding Behaviour**

Mireia Montaner[1], Jo E Lewis[1], Jessica Denom[2], Christophe Magnan[2], Hirac Gurden[2], Fiona Gribble[1], Frank Reimann[1]

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The olfactory bulb (OB) is the sensory structure that processes food odours and plays a fundamental role in the appreciation of food palatability. Within the OB, glucagon-like peptide-1 (GLP-1) receptor (GLP-1R) is expressed in the main output neurons ($OB^{GLP\text{-}1R}$). Moreover, a specific population of OB interneurons has been identified as GLP-1-producing preproglucagon (OB^{PPG}) cells. Several studies support the existence of a functional and physiologically relevant GLP-1 system within the OB. However, how food odours influence $OB^{GLP\text{-}1R}$ driven neurocircuits and how these circuits modulate feeding behaviour is unknown. To investigate the proposed relationship between OB GLP-1 and food odours, and assess its effects on feeding behaviour, we combined a standard olfactory behavioural approach with pharmacological manipulation, chemogenetics and *in vivo* Ca^{2+} imaging. Experiments were conducted on lean and diet-induced obese mice. During fiber photometry recordings, the presentation of food odours triggered a rapid increase in Ca^{2+} levels in OB^{PPG} neurons of lean mice. Gq-DREADD activation of OB^{PPG} neurons in lean mice reduced the latency to locate a hidden chocolate pellet underneath a layer of bedding, suggesting enhanced olfactory-guided behaviour. Subsequent consumption of the pellet was decreased. Similarly, a local OB injection of the GLP-1R agonist Ex-4 in obese mice also reduced the latency to find the hidden chocolate. Furthermore, activation of Gq-DREADDs in $OB^{GLP\text{-}1R}$ cells during refeeding tests led to a reduction in both chow and high-fat diet intake in obese mice. These findings suggest a role for GLP-1/GLP-1R in the OB in sensory detection of food and feeding behaviour, highlighting the influence of specific$OB^{GLP\text{-}1R}$-driven neurocircuits in food perception and consumption.

12:55 **Olfaction And Feeding Behaviour: NEuronal Substrates Underlying Odour Modulation Of Neuronal Circuits Regulating Food Intake**

Louise Eygret[1], Morgane Martin[1], Alexandra Sere[1], Farha Bouteldja[1], Vincent Simon[2], Daniela Cota[2], Xavier Fioramonti[1], David Jarriault[1]

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Maintaining a stable body weight is a challenge for a growing part of the population, and current pharmacological treatments can come with side effects. The olfactory system plays a key role in nutrition and could offer a non-invasive alternative for regulating eating behaviour. Food intake is mainly controlled by hypothalamic AgRP (orexigenic) and POMC (anorexigenic) neurons, which can rapidly respond to food cues before consumption, suggesting a sensory influence. We hypothesize that appetitive odorant molecules modulate the activity of hypothalamic neurons, providing an olfactory-driven mechanism regulating food intake. We identified bacon and peanut butter as attractive odorants for male and female mice based on investigation times. These odorant molecules revealed a potent appetitive effect in automated food intake monitoring experiments. Patch-clamp electrophysiological recordings from brain slices of mice exposed to these odorants during 30 min showed that they induced decreased firing in POMC neurons. No effect was observed on AgRP neuron activity. In vivo fiber photometry showed a modulation of POMC and AgRP neuron activity during active sniffing of the attractive odorants. These odorants induced an instant decrease in AgRP neuron activity and an increased activity in POMC neurons. Our results suggest that attractive food-related odours modify the electrical activity of neurons within the melanocortin network, emphasizing the sensory modulation of hypothalamic feeding regulation. Future work will map the involved projections between the olfactory system and the hypothalamus. Understanding how olfactory cues influence hypothalamic circuits will be useful for developing safer, innovative therapies for energy balance disorders.

1:10 **Glp-1 Receptor Agonists Significantly Impair Taste Function**

Richard Doty[1], Rafa Khan[1]

[1]University of Pennsylvania, Philadelphia, PA 19104, PA, United States, [2]University of Pennsylvania, Philadelphia, PA 19104, PA, United States

Over 10% of the US population are prescribed glucagon-like peptide-1 receptor agonists (GLP-1 RAs) to combat obesity. Although they decrease cravings for foods, their influence on chemosensory function is unknown. We employed state-of-the-art quantitative taste and smell tests to address this issue. The 53-item Waterless Empirical Taste Test (WETT®) and the 40-item University of Pennsylvania Smell Identification Test (UPSIT®) were completed by 46 persons taking GLP-1 RAs and 46 controls matched on age, sex, smoking behavior, and COVID-19 infection histories. Data were analyzed using analyses of variance. The WETT® scores were significantly diminished in the GLP-1 RA group relative to controls [total means (95% CIs) = 28.61 (25.66,31.56) and 40.63 (38.35,42.91), $p < 0.001$, $\eta 2 = 0.37$]. Eighty five percent of the GLP-1 subjects scored worse than their individually matched controls. All 5 WETT® subtest scores were similarly affected (ps <0.001). Smell function, although slightly decreased on average, was not significantly impacted ($p = 0.076$). Women outperformed men on all tests. Remarkably, UPSIT® and WETT® scores were higher, i.e., better, in those reporting nausea, diarrhoea, and other GLP-1-related side effects. This study demonstrates, for the first time, that GLP-1 RAs alter the function of a major sensory system, significantly depressing the perception of all five basic taste qualities. The physiologic basis of this effect is unknown but may involve GLP-1 receptors in the brainstem and afferent taste pathways, as well as vagus nerve-related processes

1:25 **Agrp Neurons Distinguish Oral Sugars From Sweeteners**

Misgana Y Ghidewon[1,2], Laryssa O Coutinho[2], Milena S Almeida[2,] , Sevinch Rakhmonova[2], Alisha A Acosta[2], Amber L Alhadeff[1,2]

[1]University of Pennsylvania, Philadelphia, PA, United States, [2]Monell Chemical Senses Center, Philadelphia, PA, United States

Food intake requires intricate coordination between orosensory signaling and central feeding circuits that initiate and maintain feeding. Yet, the impact of oral sugar sensing on homeostatic feeding circuits is not fully understood. Here, we combined intraoral cannulation with *in vivo* fiber photometry in mice to understand how isolated taste cues influence hypothalamic agouti-related protein (AgRP)-expressing neuron activity. Small volumes of intraorally delivered nutrients (Ensure) robustly and transiently inhibited AgRP neuron activity (n=5, paired t-test, $p<0.05$). We next determined that oral glucose (sugar), but not saccharin (non-caloric sweet taste) inhibits AgRP neuron activity (n=14, 2-way ANOVA, $p<0.0001$). This is independent of post-ingestive signaling (n=9, paired t-test, p=ns). Furthermore, food-predicting (umami and salty) and avoided (sour and bitter) taste stimuli did not impact AgRP neuron activity (n=18, 2-way ANOVA, p=ns). This suggests that taste alone is not a salient modulator of AgRP neuron activity. Instead, sugars and sweeteners may utilize different mechanisms to modulate AgRP neuron activity. To test this hypothesis, we first reanalyzed publicly available single-cell datasets and confirmed that sodium glucose cotransporter 1 (SGLT1), which transports glucose but not saccharin, is expressed in taste receptor-expressing cells within the fungiform papillae. We then pharmacologically blocked SGLT1 and showed that this eliminated the effects of intraoral glucose on AgRP neuron activity (n=12, 2-way ANOVA, $p<0.0001$). Overall, these findings provide evidence that caloric sugar and non-caloric sweeteners are distinguished in the mouth and transmitted to AgRP neurons, a feat that has typically been ascribed only to post-ingestive signaling.

1:40 - 3:00 PM	On Own
Lunch	

3:00 - 4:30 PM	L2
Symposium 1: Exercise as a Modifier of Feeding	

Chair(s): Emily Noble

3:00 **Might Energy Expenditure And Physical Exercise Be Implicated In The Control Of Appetite In Adolescents With Obesity? (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))**
David Thivel
AME2P Laboratory, CLERMONT-FERRAND, France

Long considered as two independent sides and levers of our energy balance, physical activity and energy intake keep dialoging and interacting, impacting the control of our overall energy homeostasis and health. The present talk will try to propose an overview of the effect of physical exercise, energy expenditure and energy metabolism on appetite control, energy intake and food reward in adolescents with obesity. The behavioral but also physiological, neuro-physiological and cognitive pathways involved will be discussed and new results regarding the implication of our energy metabolism and substrate use will be presented.

3:30 **To Run Or Not To Run That Is The Question**
Kevin W Williams
Center for Hypothalamic Research, Department of Internal Medicine, UT Southwestern Medical Center, Dallas, TX, United States

Regular physical activity has profound effects on brain function, influencing cognition, mood, energy balance, and glucose metabolism. Recent studies highlight that exercise induces structural and functional changes in key metabolic circuits. These dynamic neural adaptations are associated with enhanced insulin sensitivity, appetite regulation, and improved systemic metabolism. While the precise mechanisms linking physical activity to brain-mediated metabolic benefits remain under investigation, emerging evidence suggests that key brain regions, including the hypothalamus, play a critical role in these adaptations. Understanding how exercise modulates neural activity and plasticity will provide insights into its therapeutic potential for metabolic and neurological disorders. In this presentation, I will discuss recent advances in our understanding of exercise-induced neuroplasticity, with a particular focus on hypothalamic circuits that regulate energy balance and glucose metabolism. I will highlight how exercise engages metabolically relevant neuron populations and explore how these changes contribute to improvements in metabolic health.

4:00 **Regular Intense Activity Is Associated With Lower Sweet Taste Sensitivity And Increased Sugar Intake**
Isabella Kimmeswenger[1,2], Marlies Gaider[2,3,4], Kevin Doppelmayer[1], Jakob Ley[5], Barbara Lieder[1,3,4]
[1]Institute of Physiological Chemistry, Faculty of Chemistry, University of Vienna, Vienna, Austria, [2]2 Vienna Doctoral School in Chemistry (DoSChem), University of Vienna, Vienna, Austria, [3]Christian Doppler Laboratory for Taste Research, Faculty of Chemistry, University of Vienna, Vienna, Austria, [4]Institute of Clinical Nutrition, University of Hohenheim, Stuttgart, Germany, [5]Symrise AG, Holzminden, Germany

Taste sensitivity may affect food choices. In obese individuals, micro-inflammation is suspected to reduce taste sensitivity. Since intense physical activity is also associated with increased inflammatory markers, we hypothesize that higher cytokine levels in persons that perform regular intense exercise affects the taste apparatus and consequently sweet taste sensitivity and food choices. Data concerning salivary IL-6 and urinary 8-iso-PGF2-a concentrations, body composition, sweet taste sensitivity and preferences, dietary intake of sweet food, physical activity, size and area of fungiform papillae was collected from participants (m/f) who exercise ≥6 hours per week (n=34) or ≤2.5 hours per week (n=31). Data was analyzed using PCA followed by linear regression models, Student's t-tests or Mann-Whitney-U test. Overall, 44% of cumulative proportion of variance was explained by two principal components: variables related to body composition and morphological aspects of fungiform papillae were summarized in PC1, while sweet taste sensitivity, consumption of sweet foods and salivary IL-6 concentration contributed mainly to PC2. Group comparisons for the variables demonstrated that the active group had on average higher salivary IL-6 concentrations and a decreased sweet taste sensitivity, accompanied by a higher consumption of sweet foods. In addition, the active participants had 25±5% less fungiform papillae compared to less active participants. In conclusion, the results support the hypothesis that regular intense physical activity affects the taste apparatus, possibly via increased cytokine levels. The reduced sweet taste sensitivity in highly active persons may facilitate an increased sugar intake, assisting the supply of elevated energy needs for carbohydrates

3:00 - 4:30 PM	L1
Oral Session 3: Oh to be young; early life food perception and eating	

Chair(s): Kellie Tomashiro

3:00 **Measurement Of The Reinforcing Value Of Food In Infancy**
Amanda K Crandall[1], Ashley N. Gearhardt[2], Alison L. Miller[3], Katherine L. Rosenblum[4], Julie C. Lumeng[1]
[1]Departments of Pediatrics University of Michigan Medical School, Ann Arbor, MI, United States, [2]Department of Psychology, University of Michigan College of Literature, Science, and the Arts, Ann Arbor, MI, United States, [3]Department of Health Behavior & Health Equity, University of Michigan School of Public Health, Ann Arbor, MI, United States,

[4]Departments of Psychiatry and Obstetrics & Gynecology, University of Michigan Medical School, Ann Arbor, MI, United States

The reinforcing value (RRV) of food is thought to have genetic origins and emerge during infancy. Using a standardized task, the current study examined the developmental progression of the RRV of food from 9 to 12 months. 175 infants were offered, in counterbalanced order, the opportunity to press a lever for food and a block to play with. The presses required to win the reinforcer progressed by 2 after each round. The mother completed surveys on the child's appetite that were appropriate for the age point. Regression analyses controlling for order of presentation revealed that RRV, operationalized as the number of presses for the highest schedule completed, for food and nonfood reinforcers were positively associated with one another within (9m, β=0.40, p<.001; 12m, β=0.49, p<.001), but not across timepoints (p>.05). The RRV of food was associated with both weight for length z-score (β=0.18, p=.011) and conditional weight gain (β=0.09, p=0.033) at 12, but not 9 months. Likewise, the proportion of presses for food was associated with the child's score on the CEBQ enjoyment of food (β=0.56, p=.020) and satiety responsiveness (β=-0.85, p=.002) scales at 12 months. Counterintuitively, RRV at 9 months was associated with lower general appetite scores on the BEBQ (β=-0.22, p=.016). These findings suggest that although a 9-month-old infant may respond to an RRV task, their responses do not equate to the eating behavior or growth in the way they do among older infants, children, and adults. This pattern emerges closer to 12 months, perhaps because the infant is moving into a developmental phase marked by a much greater proportion of their caloric intake from the solid foods used in the task.

3:15 **&Ldquo;Cookies Make Me Feel Like Life Is Good&Rdquo;: Food-Related Emotional Expectancies In Children And Adolescents**

Jenna R. Cummings[1], Maddy Roberts[1], Ashlin James[1], Mabel S.F. Kouk[1], Aimee E. Pink[2], Julia M.P. Bittner[3], Albert Lee[4], Bobby Cheon[3], Leah M. Lipsky[3], Tonja R. Nansel[3]

[1]University of Liverpool, Liverpool, United Kingdom, [2]Agency for Science, Technology and Research (A*STAR), Singapore, Singapore, [3]Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD, United States, [4]Nanyang Technological University, Singapore, Singapore

Rationale. Modifying influences on eating behaviours early in life could prevent disease. Food-related emotional expectancies are predictions about how foods affect emotions. In adults, positive discretionary-food expectancies (e.g., "*I expect to feel happy while eating pizza*") drive intake of less healthful foods and are modifiable; however, this is unexamined in young people. We investigated food-related emotional expectancies in children (6 years) and adolescents (14-17 years). **Hypothesis.** Positive discretionary-food expectancies would predict less healthful food choices. Given that core-food expectancies (e.g., "*I expect to feel happy while eating apples*") are unrelated to eating behaviours in adults, we had no hypothesis about those expectancies. **Participants.** 78 children and 1248 adolescents. **Procedures.** Children completed (1) free-word association, saying their first thoughts in response to food prompts, (2) the Anticipated Effects of Food Scale (AEFS) for Children, and (3) eating a meal and snacks under observation. Adolescents (1) answered the AEFS for Adolescents and (2) chose between foods varying in healthfulness online. **Results.** Even 6-year-old children held strong food-related emotional expectancies (e.g., "*Cookies make me feel like life is good*," "*Bananas make me feel weird*"). Positive discretionary-food expectancies were associated with less healthful food choices in children and adolescents (medium effect sizes). Positive core-food expectancies were associated with more healthful food choices (medium effect sizes). **Conclusions.** Positive discretionary-food expectancies may reinforce unhealthful food choices across the lifespan, while positive core-food expectancies may promote health specifically in young people.

3:30 **Working Memory Moderates The Relationship Between Attentional Bias And Eating Behavior**

Jessica H. Liu[1], Afroditi Papantoni[2], Kyle S. Burger[2]

[1]The University of North Carolina at Chapel Hill, Chapel Hill, NC, United States, [2]Monell Chemical Senses Center, Philadelphia, PA, United States

Impaired working memory (WM) and attentional bias towards food have independently been associated with aberrant eating behavior patterns and elevated weight. Here, we hypothesize lower WM and higher attentional bias would be related to faster energy eating rates, increased kcal intake, and higher body mass. In this cross-sectional study, a 2-step nback (WM) and a food ad eye-tracking paradigm (time to first fixation bias on food, TTFF; total ad duration bias) were assessed in children (n=38; F=17; age=8±1.65). The eye-tracking paradigm was presented as a YouTube video with pop-up ads depicting food and toy pictures. Food intake (total kcals) and energy eating rate (kcals/min) were assessed via an *ad lib* taste test of 6 ultra-processed snacks, e.g., Oreos. Adjusting for confounds, ANOVAs were used to test for WM*attentional bias interactions with significance set to p<0.05. WM moderated the relation between TTFF and kcals consumed, where lower WM and faster TTFF were related to higher kcal consumption (p=0.057). We also observed faster TTFF was related to increased eating rate (p=0.06). No significant interactions or main effects were seen with ad duration bias (p>0.05). This suggests that implicit attentional bias (vs. sustained attentional bias) for foods plays a larger role in influencing ingestive behavior, possibly through largely unconscious processes. Further, those with poorer WM may be more susceptible to food cue-potentiated overconsumption. Further research is needed to understand the role of WM and attentional bias on food and eating behavior. Future healthy eating interventions, such as cue-reappraisal approaches, should consider individual differences in WM to tailor their intervention.

3:45 **Using Machine Learning To Identify Task Fmri Predictors Of Appetite Ratings And Weight Status In Adolescents**

Trinity Cheng[1], Liuyi Chen[1], Afroditi Papantoni[2], Susan Carnell[1]

[1]Johns Hopkins University School of Medicine, Baltimore, MD, United States, [2]Monell Chemical Senses Center, Philadelphia, PA, United States

Food cue responsiveness is thought to influence body weight. Task fMRI studies have identified brain regions activated by exposure to food cues. However, the degree to which responding within these regions is capable of predicting subjective appetite and body weight is unclear. We applied machine learning models to fMRI food cue reactivity task data from 77 adolescents (16.3±1.27y; 37M 40F; BMIz=0.64±1.21) to test whether BOLD responses to high energy-density [ED] food vs. non-food images could classify participants into groups based on subjective appetite ratings in response to high-ED foods (top 25% vs. bottom 75% on wanting (assessed during scan) and liking (assessed outside scanner)), and weight (overweight/obesity [OV/OB] vs. healthy-weight). To identify regions of interest [ROIs] we used NeuroQuery, an online

meta-analysis tool based on 13,459 neuroimaging studies, to create statistical maps of activation associated with six terms: *appetite*, *eating*, *diet*, *food*, *hunger*, *obesity*. Peak cluster coordinates (z-score>3) were identified within all six maps and used to assemble a set of 45 6-mm spherical ROIs. Mean beta values representing BOLD responses to high-ED vs. non-food images were extracted from each ROI. A supervised Random Forest algorithm with 5-fold cross-validation showed limited performance in classifying top 25% wanting (57.14% accuracy, 61.88% AUC), top 25% liking (75.32% accuracy, 57.53% AUC), and OW/OB status (59.74% accuracy, 64.43% AUC). These preliminary models suggest low power of BOLD responses within our selected ROIs to predict subjective appetite and weight in our sample. Future work will consider alternative feature selection methods and whole brain connectivity approaches in larger samples with more variance in weight/eating phenotypes.

4:00 **Maternal Prebiotic Supplementation Improves Vagal Function And Diet Induced Obesity In Offspring**

Jennifer M. Houston[1], Jillian M. Allen[2], Rachel E. Lippincott[2], Eden E. Crain[2], Jung H. Byun[2], Dulce M. Minaya[2], Kellie L. Tamashiro[3], Claire B. de La Serre[1]

[1]Colorado State University, Fort Collins, CO, United States, [2]University of Georgia, Athens, GA, United States, [3]Johns Hopkins University, Baltimore, MD, United States

Maternal obesity increases risk for metabolic disorders in offspring. Gut-innervating vagal afferents terminate in the nucleus of the solitary tract (NTS), conveying post-ingestive cues to regulate meal size. Rat pups born to high fat (HF) diet-fed dams show reduced sensitivity to gut satiety peptides and post-prandial NTS activation linked to altered feeding. A HF-type gut microbiota is necessary and sufficient to alter vagal structure and function. We hypothesized that improving microbiota composition in HF-fed dams will enhance offspring gut-brain communication. Sprague-Dawley dams were fed a chow (LF), HF, or high fat supplemented with prebiotics (resistant starch, RS, HF+12% RS) diet during pregnancy and lactation. Offspring were weaned onto a LF diet. By post-natal day 14 (P14), HF offspring were heavier than HFRS ($p<0.05$) and LF ($p<0.05$) pups. Immunostaining of NTS at P21 showed a decrease in vagal innervation in HF pups compared to LF and HFRS offspring. This was inverted in adulthood but did not improve function, as HF offspring failed to reduce food intake in response to gut satiety peptide cholecystokinin (CCK, 1.5ug/ml/kg). This was rescued in HFRS pups, associated with a reduction in meal size and indicating improved vagal function. When challenged with a HF diet, HF pups gained significantly more weight than HFRS offspring ($p<0.05$), highlighting protective effects of maternal supplementation. This may be limited to gut-originating signals as both HF and HFRS offspring displayed a deficit in NTS leptin signaling compared to LF pups. We concluded that maternal HF diet alters vagal communication in offspring, increasing risk for diet-induced obesity. Some effects appear to be microbiota driven and improved with maternal RS supplementation.

4:15 **Effects Of Semaglutide Injections On Weight And Body Composition In An Adolescent Rodent Model.**

Austin M. Mills, CJ Petty, Emily E. Noble
University of Georgia, Athens, GA, United States

Glucagon like peptide receptor (GLP-1R) agonists are key players for treating obesity, and some are FDA approved for use in adolescents as young as twelve; however, the long-term developmental effects are unknown. We investigated the effects of the GLP-1R agonist semaglutide (sema) in a rodent model of adolescent obesogenic diet consumption and hypothesized that sema would reduce weight gain and growth. Male and female adolescent Sprague Dawley rats (PND 28) were fed a high fat, high sugar diet alternating between 60% kcal from fat and 45% kcal from fat as well as an 11% high fructose corn syrup solution where flavored and unflavored drinks were offered on different days (HFHS; n=8/sex). Rats on the control diet (CD; n=8/sex) were fed standard chow with two bottles of water. Data were analyzed using 3-way ANOVAs for body weight and 2-way ANOVAs for body composition, or t tests for body composition between diet groups; $\alpha<0.05$ was considered statistically significant. Compared with CD, there was a significant increase in body fat percentage in both male and female HFHS-fed rats within one week. Rats were sub-divided to receive daily injections of sema (70 μg/ml) or vehicle (n=4/group per sex). Female rats treated with sema showed reduced weight gain driven by reductions in body fat in diet both groups. In contrast, sema-treated male rats showed reduced weight gain due to reduced lean mass and length growth. These studies elucidate a sex difference in adolescent responses to sema, which may be due to the timing of puberty relative to introduction of sema (a topic of ongoing investigation). Given that sema is already in widespread use, these findings have important clinical implications.

4:30 - 5:30 PM	North & South Mezzanines
Poster Session 2, Exhibits & Coffee Break	

Poster numbers 100-146 are located in the South Mezzanine. Poster numbers 147-184 are located in the North Mezzanine.

P102 **Navigating Novelty: The Role Of Arousal In The Approach And Avoidance Of Novel Foods**

Zhen An, Catherine A. Forestell
William & Mary, Williamsburg, VA, United States

Food neophobia (FN), defined as an avoidance or lack of approach to new foods, is common among adults. Previous research has suggested that food novelty may induce high arousal, which may underlie food rejection in FN. To test this, young adults (N=102) completed an experimental task over two days, separated by one week. On each day, they viewed eight pairs of identical food images labeled with either familiar or unfamiliar names, presented in random order, while their pupil dilation (physiological arousal) was measured. Perceived negative arousal to each food was assessed using a 7-point rating scale (1 = 'Not at all anxious' to 7 = 'Very anxious'). Finally, participants' approach/avoidance motivations to new foods were measured using the Motivation to Eat New Foods scale (MENF). Linear mixed-effects models were employed, with motivations and familiarity as fixed effects and arousal as the dependent variable. Regarding perceived arousal, greater avoidance motivation was linked to heightened arousal ($F(18,83) = 2.04$, $p = 0.016$), with this effect being more pronounced for unfamiliar foods ($F(18,83) = 2.09$, $p = 0.013$). In contrast, higher approach motivation was associated with greater pupil dilation ($F(19,82) = 1.87$, $p = 0.027$), an effect that was not influenced by food familiarity. These findings indicate distinct patterns: motivation to approach new foods appears to be associated with physiological arousal, potentially reflecting positive affect or excitement when viewing foods, regardless of familiarity. In contrast, motivation to avoid foods appears to be linked with increased perceived negative arousal, especially in response to new foods. Understanding arousal in FN may help develop interventions to improve dietary variety and quality in food-neophobic individuals.

P104 **County-Level Implicit Food Palatability Associations Mediate The Relationship Between Local Food Environments And Obesity Rates**

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Implicit associations (IA) are spontaneously activated attitudes in response to a stimulus (e.g., food) that are learned from the social environment. Aggregated IAs, such as across a county, are theorized to reflect regional-level societal biases. While relationships between regional IAs and social biases have been examined (e.g., IAs about demographic groups and regional health disparities), there have been no investigations of links between regional food-related IAs and obesogenic environments. The promotion of IAs favoring palatable energy-dense foods could be one mechanism by which obesogenic environments increase risk of poor metabolic health. We tested this by extracting individual IAs favoring the taste of unhealthy (vs. healthy foods) based on the Implicit Association Test, as well as explicit self-reported attitudes of oneself as a healthy eater from a large U.S. dataset (Project Implicit Health; 11,504 individuals across 1,339 counties). We tested whether average IAs and self-reported healthy eating mediate the relationship between the food environment (density of fast-food outlets and grocery stores; Food Environment Atlas) and obesity/diabetes rates (U.S. Diabetes Surveillance System) on a county level. There was an indirect effect of county-level unhealthy food-favoring IAs (but not self-reported healthy eating) on the relationship between county fast-food density and obesity rates ($b = 0.11$, 95%CI: 0.05, 0.27). No indirect effects were observed for grocery store density as a predictor or diabetes rates as an outcome. These findings suggest that obesogenic properties of local environments, like higher accessibility or salience of fast-food, may affect health by shaping implicit food-related attitudes of people situated within these environments.

P106 **Debating As A Tool For Shaping Attitudes And Food Choices: The Role Of Debate Composition In Attitudes And Meat Consumption Change**

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Rationale: Despite a consensus within the scientific community in favor of meat consumption reduction (MCR), actual changes in the population are limited. Minipublic debates (MPD), i.e. supervised debates in small groups where participants receive information on the subject, can induce attitude changes among participants. This study aims to test the effect of participation in MPD about the place of animal and plant-based foods in our diet on participants' MCR and attitudes. Can MPD induce changes in attitudes and behaviours? Does the initial attitude divergence amongst debating participants matter? **Hypotheses**: We expect participants with negative views (PNV) towards MCR in the mixed debate condition to become more supportive of MCR and more likely to accept the reduction challenges than PNV in other conditions. **Procedures**: 600 participants will participate in online MPD. Participants' attitudes, consumption intentions and meat consumption will be measured before and after the MPD. Red- and transformed- MCR challenges will be proposed after the MPD. Depending on their initial attitudes, participants will be randomly allocated to 1 of the following 3 conditions: -Mixed debate, where PNV and participants with positive views (PPV) about MCR will debate together; -Homogeneous debate (HD), where PNV will debate together; -No debate, where PNV and PPV will tackle the subject alone without debating. Mixed linear and logit regressions will be used to assess the effects of debate group composition on attitudes and commitments to MCR. **Preliminary results (half sample)**: PNV become more supportive of MCR in all conditions, this trend is less marked in the HD condition than in other conditions. **Conclusion**: Group composition alters MPD potency to moderate attitudes of PNV.

P108 **Deciding When To Introduce Meat To Infants And Toddlers: Factors Influencing Caregivers' Choices**

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Although iron and zinc are essential nutrients for growth and development, their intake is below recommended levels in more than half of breastfed infants in the US. The 1st Foods Study identified factors associated with caregivers' decisions about when to introduce meat, a food rich in iron, zinc, and other micronutrients, to their children. Caregivers (N=445) of children between 6-24 months from across the US completed an online survey, during the spring of 2022, assessing caregiver-, child-, and family-related characteristics, and decisions about introducing meat during complementary feeding. Caregivers who had introduced meat to their children (n=312) reported that meat was introduced when children were almost 9 months of age (*Mean*=8.8, *SE*=0.2). In general, meat was introduced later than other types of foods. Almost two-thirds (62%) of caregivers indicated that they had offered meat because their child was showing interest in it. About half (54%) indicated that their child was chewing other solid foods and seemed ready to try meat, and some waited until their children had teeth (39%). Analyses of Covariance, which controlled for child age, revealed that compared to caregivers who had offered meat to their children, those who had not were less attached to meat (p<0.001), more food avoidant (p=0.031), and breastfed longer (p=0.026). Children who had not been introduced to meat were fussier eaters (p=0.008) and enjoyed food less (p=0.003). Delaying the introduction of meat raises questions about the adequacy of children's iron and zinc intake, especially for those who breastfeed. Understanding factors predicting caregivers' decisions about when to introduce meat can aid in developing innovative strategies to ensure adequate nutrition for young children.

P110 **Association Between Food Chewing Features And Weight Status Among Israeli Adolescents**

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Rationale/Premise: Adolescents' weight gain is influenced by multiple factors, including dietary habits. Chewing characteristics, such as chewing speed and duration, have been explored in relation to weight status, but findings remain inconsistent due to varying measurement methods and study designs. Understanding the association between food chewing features and weight status may provide valuable insights into dietary behaviors contributing to excess weight. **Hypothesis:** Among adolescents, higher consumption of foods requiring increased chewing effort will be positively associated with a higher BMI Z-score. **Species:**Human **Number of Subjects:** 3,428 adolescents **Procedures:** We analyzed secondary data from the Israeli National Health and Nutrition Survey collected from 2015–2016 among grades 7–12 students. Food Frequency Questionnaires (FFQs) were used to assess dietary intake. A panel of four registered dietitians specializing in pediatric nutrition classified the chewiness of foods from the FFQs. Multivariable logistic regressions examined the association between food intake across chewiness levels (separately per level) and weight status, adjusted for age, sex, socioeconomic status, ethnicity, and mean daily energy intake. **Results:** For every 10-gram increase in intake of level 2 of chewiness, the odds of overweight or obese (BMI z-score≥1) weight status increased by 0.3%. For levels 3 and 4, the odds increased by 0.7% per 10-gram increase. **Conclusions/Relevance:** The findings suggest that food chewiness is associated with weight status among adolescents. This study underscores the importance of further exploring the role of chewing behaviors in weight management among adolescents and their potential implications for targeted dietary interventions.

P112 **Impulsivity Moderates The Relationship Between Early Life Adversity And Child Food Intake And Eating Behaviour**

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Rationale. Early-life adversity (ELA) increases the risk of metabolic and mental disorders, potentially influencing health outcomes through disrupted eating behaviours. However, susceptibility to ELA varies, and the factors that cause these differences remain unclear. Given the role of impulsivity in both psychopathologies and metabolic disorders, altered executive function may predispose individuals exposed to ELA to maladaptive eating behaviours. **Hypothesis.** ELA is associated with altered food intake and eating behaviours, particularly in high impulsive children. **Methods.** In the MAVAN cohort (n=91), ELA was assessed as a composite score, impulsivity via the Snack Delay Task at age 3, food intake at age 4 (Food Frequency Questionnaire, Snack Test), and eating behaviour at age 6 (Child Eating Behaviour Questionnaire). Linear regression models included an interaction term between adversity and impulsivity, adjusted for income and BMI z-score.

Simple slope analyses tested the adversity-outcome association at the 5^{th}, 50^{th}, and 95^{th} percentiles of impulsivity (P<0.05). **Results.** ELA interacted with impulsivity to influence food intake at age 4 and eating behaviour at age 6. Boys exposed to ELA with high impulsivity at age 3 had greater total and saturated fat intake, higher eating rates (calories/min), and increased emotional overeating. In girls, high ELA was linked to greater sugar intake in those with high impulsivity. **Conclusions.** These findings suggest that impulsivity moderates the impact of ELA on childhood food intake and eating behaviour. Identifying these interactions may help develop targeted interventions for individuals most vulnerable to adversity´s long-term health effects.

P114 **Advanced Ai Technology And Photo Recognition-Based Smartphone App (Syft Health) Improves 7-Day Adherence To Dietary Self-Monitoring And Diet Quality Compared To 24-Hour Dietary Recall And My Fitness Pal.Advanced Ai Technology And Photo Recognition-Based Smartphone App (Syft Health) Improves 7-Day Adherence To Dietary Self-Monitoring And Diet Quality Compared To 24-Hour Dietary Recall And My Fitness Pal.**

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Adherence to daily dietary self-monitoring is the strongest predictor of dietary change and weight loss in behavioural weight-loss interventions. However, standard tracking systems (digital and otherwise) are burdensome, leading to substantial decreases in adherence over time. The advent of AI in recent years has led to the development of advanced picture recognition systems that can decompose ingredients and items to allow for seamless dietary tracking and monitoring, potentially improving adherence. Here, we tested the efficacy of a new AI-based diet tracking app (Syft) compared to standard dietary self-monitoring apps and tools on 7-day adherence and diet quality. Participants aged 18-55 (*M=25.07)* were randomly assigned to one of three different self-monitoring modalities: (1) standard 24-hour dietary recall; (2) My

Fitness Pal; (3) Syft. Across the 7-day monitoring period, participants assigned to the Syft group logged significantly more meals (M=4.45) compared to the 24-hour recall (M=1.62) and My Fitness Pal (M=2.26) groups (F(12,912) = 5.295, p<.001, d=.320). Latent growth curve analyses indicated that individuals assigned to the 24-hour dietary recall and My Fitness Pal group showed transient decreases in adherence over the 7-day period, whereas, adherence remained consistent in the Syft group. Further, while there was no difference in kcal consumed across groups (p=.123), participants in the Syft group reported consuming more fibre (p<.001), protein (p=.011), and fruits and vegetables (p=.001) than those assigned to the 24-hour recall and My Fitness Pal groups. Collectively, findings suggest that AI-assisted photo recognition apps can reduce the burden of dietary self-monitoring, improving adherence and diet quality.

P116 **Stress, Emotional Eating, And Sensitization To Food Reinforcement: Examining Adolescent Responses To Repeated Exposure**

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Introduction: Emotional eating (EE) refers to overeating in response to emotional cues, while sensitization involves an increased willingness to seek food after repeated exposure. EE is associated with disordered eating, but its role in food reinforcement is less understood. This study investigates how emotional eating, specifically its subscales, interacts with stress to influence sensitization to food reinforcement in adolescents. **Methods:** A total of 118 adolescents (M age = 11.7) completed assessments of EE, stress (PSS), and disordered eating (EDE-Q Global). Sensitization was calculated as the difference in the reinforcing value of food before and after two weeks of daily snack food intake. A multiple regression model examined the independent and interactive effects of EE, PSS, and EDEQ on sensitization. **Results:** Results showed that EE, particularly the Unsettled and Depression subscales, was negatively associated with sensitization. There was also an interaction of the depression subscale of EE and PSS scores, with the relationship with sensitization changing from negative to positive. However, disordered eating was not associated with sensitization, even in the adjusted model. **Conclusions:**These findings underscore the importance of considering EE and stress interactions in understanding sensitization of the reinforcing value of food in adolescents. Interventions that address EE and stress management could help reduce the reinforcing value of food and sensitization

P118 **Cue-Triggered Food-Seeking Varies With The Estrous Cycle In Obesity-Prone Rats: Insights Revealed By Machine-Learning Based Analysis With Labgym**

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In people, environmental cues that signal food availability can powerfully influence eating and contribute to diet-induced obesity. In selectively bred obesity-prone (OP) and obesity-resistant (OR) rats, food cues evoke greater food cup approach in anticipation of food in OP vs OR rats, and this approach varies with the estrous cycle only in OPs. Here, we examined how food cues influence food-seeking (i.e., lever pressing) in OP and OR females across the estrous cycle with the expectation that OPs would show greater cue-evoked food-seeking than ORs during metestrus and diestrus (M/D). In addition to traditional automated measures (number of food cup entries or lever presses), we used the machine-learning based analysis tool, LabGym, to train a model to identify and categorize naturally occurring (e.g., locomotion, rearing) and food-seeking (e.g., food cup digging, lever biting) behaviors. This enabled us to quantify varying intensities of cue-evoked motivation. Results from traditional measures indicate that food cues enhanced food-seeking to a similar degree in OP and OR females (i.e., lever-pressing in response to the food cue was similarly elevated, n=31 OP/ 20 OR). However, LabGym analyses revealed that OPs spent more time interacting with the lever (pressing and biting) during the food cue than ORs. OPs also spent more time engaged in cue-induced food cup behaviors (e.g., food cup digging). Thus, the intensity and vigor of cue-evoked food-seeking was greater in OPs than ORs. Furthermore, both analyses revealed effects of the estrous cycle on cue-induced food-seeking only in OPs. These data will be discussed in light of susceptibility to weight gain, and the development of machine-learning tools like LabGym to provide novel insights in behavioral analysis.

P120 **Adolescents&Rsquo; Perceptions And Use Of Ai Chatbots For Health And Wellbeing Information**

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AI chatbots (e.g. ChatGPT) are increasingly used in everyday life. Their human-like communication encourages various interactions, including answering questions around health and wellbeing. Adolescents have been particularly open to this new technology, often using it for learning. However, it is unclear whether they are using AI chatbots to seek information about health and wellbeing. Our objective was to explore, via an online survey, how adolescents use AI chatbots to seek out information around health and wellbeing. Facilitated by secondary schools, adolescents (11-16 years; N=577) completed an online survey which asked about their online activity, perceptions and use of AI chatbots, and accessing resources about health and wellbeing. Those who reported having used AI chatbots to find out about health and wellbeing answered open-ended questions about their experiences. Most adolescents (91%) had heard of AI chatbots. Many (42.5%) reported they would feel confident using AI chatbots to find health and wellbeing information. Almost a third (30.2%) had previously done this, with 23% asking about eating/nutrition, appearance, fitness, or mental health. Those who had used AI in this way previously were more confident using AI for this purpose and rated it as more trustworthy and helpful than those who had not. Further analyses to investigate individual differences in use and perceptions of AI chatbots will be discussed. The findings of this research will help to shed light on the way that adolescents are interacting with AI for health information. This is important not only for informing effective interventions to raise digital literacy and awareness around AI, but in understanding how to best get effective health and wellbeing information to this group.

P122 **Investigating The Efficacy And Feasibility Of Manipulating Mindful Eating Practices On Food Intake In Humans**

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To develop effective mindful eating interventions, it is essential to identify which practices affect food intake. Our previous systematic review (PROSPERO CRD42022346160) and online study (https://osf.io/d2cj3) highlighted two practices associated with reduced food intake and lower BMI: 'present moment awareness of the sensory properties of food' and 'attention regulation' (sustaining focus on food and preventing mind-wandering). We report two studies evaluating the efficacy of these practices in reducing food intake and their feasibility in free-living humans. In Study 1 (laboratory experiment), participants (N=135) attended two sessions a week apart. In each session they ate a cookie with different instructions. Instructions focused on how the cookie was baked (control) or one of three mindful eating instructions: i) to pay attention to the sensory properties of the cookie, ii) to keep attention focused on the cookie, or iii) both instructions combined. Afterwards, an *ad libitum* taste test measured cookie and crisp intake. Medium effect sizes indicated that the attention regulation (η^2=.06) and combined instructions (η^2=.08) reduced food intake. The sensory properties instruction had no effect (η^2=.00). In Study 2 (free-living trial), participants (N=60, 55 completed) are provided with NHS dietary advice or NHS dietary advice with the combined mindful eating instructions from Study 1 and asked to follow the advice at each meal/snack for 14 days. Participants complete video calls (Days 1 & 15) and ecological momentary assessments (Days 6 & 11) to capture feasibility outcomes (adherence, acceptability etc). Body weight change (between Day 1 & 15) is a secondary outcome. Together, these findings provide insights into the development of mindful eating interventions.

P124 **Associations Between Reproductive Hormonal Milieus And Binge Eating: The Role Of Sex And Hormonal Contraceptive Use**

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Sex hormones influence binge eating (BE) across species. Hormonal contraceptives offer a unique opportunity to examine the potential effects of exogenous ovarian hormones on BE in humans. While some studies have linked oral contraceptive (OC) use to greater BE, research has overlooked OC heterogeneity, and no study has examined hormonal intrauterine device (IUD) use and BE. In this study, we tested three a priori hypotheses regarding sex hormone influences on BE in a sample of 356 human females and 150 human males recruited from the University of Michigan Department of Psychology Subject Pool and the community. We hypothesized that: (1) females would score higher on the Binge Eating Scale (BES) relative to males, (2) BES scores would differ by hormonal milieu among females such that IUD users would report the highest BE, followed by OC users, and naturally cycling individuals with the lowest BE, and (3) among OC users, those taking pills with greater androgenic and progestational activity and lower estrogenic activity would report the highest BE. We tested these hypotheses using ANOVA and regression analyses. Results showed that females reported more BE than males, but BES scores did not differ across IUD users, OC users, and naturally cycling individuals. In an exploratory analysis, we found that BE-related factors operate differently within groups: among naturally cycling individuals and OC users but not IUD users, recruitment through the subject pool and higher BMI were associated with greater BE. OC hormonal formulation was not significantly associated with BE. Findings confirm sex differences in BE and suggest distinct BE-related profiles by hormonal milieu. Further research should explore differential susceptibility to engage in BE in a high-risk hormonal milieu.

P128 **Hindbrain Glp1R Neurons Mediate The Weight Loss And Aversion Effects Of Obesity Drugs**

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Long-acting glucagon-like peptide-1 receptor (Glp1r) agonists reduce food intake and body weight in both rodents and humans, but also cause nausea and/or vomiting in most individuals. The specific Glp1r neuron population(s) mediating these effects remains unclear. To address this, we ablated Glp1r-expressing neurons in drug accessible sites [dorsal vagal complex (DVC), arcuate nucleus (ARC), and vagal afferents] and assessed the effects of the Glp1r agonist, semaglutide, in mice. In acute experiments, DVC Glp1r neuron ablation, but not ablation of the other populations, completely blocked food intake suppression by semaglutide (n=6-7/group, all $p<0.05$ except DVC, p=ns). In a three-week study in diet induced obese mice, only DVC Glp1r neuron ablation prevented weight loss by chronic semaglutide (n=7-11/group, two-way ANOVA, $p<0.001$). Conversely, chemogenetic activation of DVC Glp1r neurons caused robust anorexia (n=7-8/group, paired t-test, $p<0.001$) and conditioned avoidance (n=6-9/group, two-way ANOVA, $p<0.01$). Next, we wanted to determine how Glp1r-expressing DVC subregions – the area postrema (AP) and nucleus tractus solitarius (NTS) – contribute to these effects. Genetic deletion of Glp1r in the AP but not the NTS blocked the formation of a semaglutide-induced flavor avoidance (n=8, two-way ANOVA, $p<0.0001$). Glp1r deletion in neither subregion was sufficient to block food intake suppression by Glp1r agonists (n=8, two-way ANOVA, $p<0.01$). Ongoing studies are examining the effects of Glp1r deletion in the AP or NTS on the ability for chronic semaglutide to promote weight loss and aversion in obese mice. Overall, these data reveal the role of hindbrain Glp1r subpopulations in mediating the weight loss and aversion effects of obesity drugs.

P130 **Melanocortin Receptors Mediate The Membrane Delimited Effects Of Corticosterone On Glutamatergic Synaptic Transmission In The Nucleus Of The Solitary Tract.**

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Circulating glucocorticoid levels are dynamic and vary with the time of day, stress, and nutrient status, all of which alter autonomic function, feeding, and energy homeostasis. Vagal afferent neurons relay viscerosensory signals and integrate circulating hormones to control autonomic function and behaviors. In the brainstem nucleus of the solitary tract (NTS) vagal terminals release the excitatory neurotransmitter glutamate to drive NTS signaling. Previously we have found that corticosterone (CORT) has robust and rapid inhibitory effects on afferent glutamate release that are mediated via a membrane G-protein coupled receptor tied to retrograde cannabinoid receptor 1 (CB-1R) signaling. The cellular effects of CORT and other steroids are best described via their action at intracellular nuclear receptors that have long lasting action on gene transcription. Steroids like CORT also have rapid, membrane delimited signaling capacity, however the identity of the membrane receptor mediating the effects of CORT remains unknown. Using acute rat brainstem slice preparations with patch-clamp electrophysiology we confirmed CORT rapidly decreased glutamatergic synaptic transmission. This inhibitory effect of CORT was phenocopied by the melanocortin 3/4 (MC3/4) agonist melanotan 2. The inhibitory effect of CORT was attenuated with the selective pharmacological blockade of MC4, but was not affected by antagonism of MC3. Antagonists at the glucocorticoid receptor were also effective at blocking melanotan 2 signaling. Taken together, these results suggest the rapid membrane delimited effects of CORT are mediated via MC4 receptors and share common binding and pharmacology with melanocortin agonists.

P132 **Effect Of An Adolescent Western Diet On The Brain And Impulsive Eating Behavior In Rodents**

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Adolescence is a critical period when environmental factors such as diet can have a long-term impact on brain function. The hippocampus, a brain region important for learning and memory, is negatively impacted by consumption of a Western Diet (WD), high in saturated fat and added sugar, and these effects have been shown to be long lasting when the WD is consumed during adolescence. The hippocampus also regulates eating behaviors such as food impulsive behavior. Therefore, we hypothesized that an adolescent WD consumption increases food impulsive behaviors. Twenty-four male Sprague Dawley rats were fed either a WD (n=12) containing a high fat diet (Research Diet D12451) along with an 11% high fructose corn syrup solution during the adolescent phase of development, or a standard chow control diet (CD; n=12). Once animals reached adulthood, all animals were fed standard chow diet so that we could isolate the effects of the WD during adolescence on the brain. The Differential Reinforcement of Low Rates of Responding (DRL) task was used to test impulsive action for sucrose. Data were analyzed using two-way ANOVAs with Holm Sidak post hoc analyses ($P<.05$ considered significant). There was a time x diet interaction with a main effect of time and diet, where WD-fed animals had higher caloric intakes and body weights compared to CD. WD during adolescence did not increase impulsive responding for sucrose in male rats during either the fed or fasted conditions. Preliminary data in female rats (n=8/group) suggests that an adolescent WD does increase impulsive responding for sucrose in female rats, but females were more impulsive for sucrose in general. Ongoing experiments will determine how WD exposure in adolescence impacts other hippocampal-dependent feeding behaviors.

P134 **Effects Of Western Diet On Recognition Memory And Neural Activation In Middle-Aged Rats**

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Normal aging is associated with cognitive decline in both humans and rodents. A Westernized diet (WD), high in saturated fats and sugars, has been implicated in promoting premature aging and accelerating cognitive deficits. Both aging and WD consumption have been linked to impairments in Novel Object Recognition (NOR) memory, which relies on the dorsal hippocampus (DH), medial prefrontal cortex (mPFC), and retrosplenial cortex (RSC). While previous research has primarily focused on young animals and short-term memory retention, the effects of WD on memory consolidation in middle-aged males and females remain unclear. This study investigated NOR memory in middle-aged (9–10 months) male and female rats fed either a chow diet (CD) or WD. Memory was assessed using short (4-mins) and long (24-hrs) retention intervals. Additionally, expression of zif268, a neural activation marker, in the DH, mPFC, and RSC was measured to explore potential mechanisms of memory consolidation. Results showed that both CD- and WD-fed females displayed intact memory at both time points. These groups also exhibited increased zif268 expression in the mPFC compared to naïve controls, but no changes were observed in the DH or RSC. In contrast, male rats in both diets performed well at 4 min but failed at 24 hrs. CD-fed males showed greater zif268 expression than WD-fed males across all regions tested and exhibited increased activation following NOR. Significant interactions between diet and testing were found in the mPFC and dentate gyrus, with only CD-fed males showing test-related increases. These findings suggest that WD may impair neural activity related to memory consolidation in middle-aged males but not females, highlighting sex-specific effects of diet on cognitive aging and memory processes.

P136 **Impact Of Maternal Obesity On Feeding Behaviour And Hypothalamic Development In Offspring: Role Of Fetal Hyperinsulinemia**

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Maternal obesity in pregnancy is linked to obesity in offspring. Our previous mouse studies have shown that offspring from obese pregnancies develop hyperinsulinemia, hypothalamic insulin resistance, and hyperphagia. However, the role of insulin in altered hypothalamic development and feeding behaviour is unclear. We hypothesise that elevated fetal insulin disrupts hypothalamic development in offspring from obese pregnancies, and is a cause of dysregulated food intake. We present results of two studies using a C57BL/6J mouse model. The first assessed 12-month-old offspring (n=16-20 males and females from lean or obese pregnancy). The second used neurosphere assays of fetal hypothalamus (n=3 lean or obese pregnancy) treated with insulin or vehicle. Body weight and food intake in adult offspring from control and obese pregnancies were assessed using fast-refeed and ad-lib feeding studies. The effect of insulin on fetal hypothalamic neural progenitor cell (NPC) proliferation was evaluated via neurosphere assays and immunofluorescence. 12-month-old offspring from obese pregnancies were significantly heavier than those from control pregnancies, despite both groups being fed an identical chow diet. Female offspring of obese dams had higher fast-induced food intake, while male offspring of obese dams showed reticence to approach food in a fast-refeed challenge but greater food intake during ad-lib feeding. Neurosphere assays showed fetal hypothalamic NPCs from obese pregnancies are resistant to the proliferative effects of insulin, in line with our previous findings of resistance in insulin signalling in the fetal hypothalamus *in vivo*. Exposure to maternal obesity in utero is associated with fetal hypothalamic insulin resistance and long-term changes to feeding behaviour.

P138 **Pasta: An Open-Source Matlab Toolbox And Protocol For Fiber Photometry Signal Processing, Transient Detection, And Trial Analysis**

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Fiber photometry (FP) is a rapidly growing technique to record real-time neural signaling in awake, behaving subjects. While several open-source tools exist to process and analyze FP data, platforms can be inflexible in accommodating experimental designs, inconsistent in signal peak detection and trial analysis, and operate through user-friendly GUIs at the cost of transparency. To remedy these challenges, we developed PASTa, an open-source FP signal processing toolbox based in MATLAB, and its user guide. To validate our pipeline, we recorded mesolimbic dopamine dynamics in rats using 4 sensors: GRABDA2H, GRABDA3M, dLight1.3b, and GCaMP6f (each n=10). By comparing several scaling and subtraction methods, we identified scaling in the frequency domain prior to subtraction outperforms regression-based approaches. After applying a bandpass filter, PASTa offers multiple options to normalize FP signals in dF/F or z-score (i.e.,

full session, session baseline, trial). Data can then be analyzed to detect individual transient events or signal by trial. While other tools use a sliding window and absolute amplitude threshold approach to detect transients, PASTa thresholds individual transients relative to pre-peak baselines, allowing for more reliable detection of transients with characterization (i.e., event amplitude, rise time, fall time, and width). PASTa hosts additional functions to detect signal magnitude and individual events by trial, across long epochs, with drug injections, and many other paradigms. The pairing of PASTa's MATLAB annotated code and user guide provides a high level of accessibility, adaptability, and transparency for users at any level. Ultimately, our toolbox introduces customizable, user-friendly platform to process FP signals and detect events.

P140 **Network-Targeted Neurostimulation Enhances Hypothalamic Functional Connectivity In Persons With Overweight Or Obesity**

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Transcranial direct current stimulation (tDCS) is a non-invasive neurostimulation approach that can influence brain function and behavior. Recent studies show the possibility to stimulate the hypothalamus-appetite network using network-targeted tDCS (net-tDCS) to influence cognitive control and food intake. However, the underlying neural mechanisms are unknown. In this study, we investigated the effect of net-tDCS on resting-state functional connectivity (FC) within this network. In a randomized, double-blind study, 17 persons with normal-weight (Nw) and 17 persons with overweight (Ow) or obesity (Ob) (sex-balanced cohorts) completed two sessions of 25-min active net-tDCS in a counterbalanced order. Active net-tDCS included inhibitory and excitatory stimulation of the hypothalamus-appetite control network. Resting-state fMRI was acquired pre- and post-stimulation.Hypothalamus-appetite network FCwas assessed between 18 predefined regions within the target network. We evaluated group (Ow or Ob vs Nw) and fMRI timepoint and group by fMRI timepoint interactions using a network-level p-FDR correction. Persons with Ow or Ob showed a trend to lower FC compared to Nw prior net-tDCS. Furthermore, a significant interaction between group and fMRI timepoint was observed. Persons with Ow or Ob showed increased FC after excitatory net-tDCS, particularly between regions involved in reward processing and cognitive control, while persons with Nw exhibited a decrease. Inhibitory net-tDCS did not yield significant effects after network-level correction. The results suggest that excitatory net-tDCS can enhance resting-state FC in the hypothalamus-appetite control network in persons with Ow or Ob. Future research should explore how these connectivity changes relate to behavioral outcomes.

P142 **In Vivo Phenotyping And Transcriptomic Characterization Of Glucose-Dependent Insulinotropic Polypeptide Receptor (Gipr) Neurocircuits Of The Paraventricular Hypothalamus**

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Despite the necessity of central glucose-dependent insulinotropic polypeptide (GIP) receptor (GIPR) expression for the weight lowering effects of GIP/glucagon-like peptide 1 (GLP-1) dual agonists, uncertainty remains regarding the appetite regulatory pathways engaged by *Gipr* neurons, and how these integrate with *Glp1r* neurocircuits. This study used mouse models to explore the connectivity, molecular profile and appetite regulatory effect of *Gipr* neurons in the paraventricular nucleus of the hypothalamus (PVH). Using viral-assisted projection mapping we found that *Gipr* neurons in the PVH ($Gipr^{PVH}$) densely innervate the NTS, median eminence and posterior pituitary—regions that are accessible to peripherally administered GIP/GLP-1 dual agonists. We explored the molecular identity of $Gipr^{PVH}$ neurons using a combination of single cell transcriptomics and RNAscope, finding that $Gipr^{PVH}$ neurons are primarily somatostatin or thyrotropin-releasing hormone (*Trh*) positive, with only 5% of $Gipr^{PVH}$ neurons expressing vasopressin or oxytocin, supporting a role for GIPR signaling in both parvocellular and magnocellular circuits. In agreement with human HYPOMAP data, we found the PVH is one of the few hypothalamic centers where incretin receptors are expressed in the same neurons, with 20% of $Gipr^{PVH}$ neurons co-expressing *Glp1r*. Chemogenetic activation of $Gipr^{PVH}$ neurons increased energy expenditure and produced sustained suppression of food intake affecting meal number, size and duration. Intersectional approaches are ongoing to characterize the relative contribution of distinct subsets of $Gipr^{PVH}$ neurons to appetite regulation and hypophyseal function, and how these circuits may intersect with GLP-1-dependent signaling.

P144 **The Interplay Between Kcnb1 Potassium Channel And Leptin Receptor In Modulating Hypothalamic Neuronal Dynamics And Ingestive Behaviors.**

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The hormone leptin modulates ingestive behaviors and energy regulation by binding to the leptin receptor (LepR) on hypothalamic neurons. It's not a coincidence that the voltage-gated potassium channel KCNB1 is found in the same hypothalamic neurons. It is well established that this channel collaborates with macromolecules at the plasma membrane to modulate neuronal mechanisms. As a new avenue, we studied the link between KCNB1 and LepR and their role in synergically regulating hypothalamic neuronal dynamics and leptin signaling. We hypothesized that KCNB1 not only can manage hypothalamic cellular dynamics alone but also by forming complexes with LepR they can together modulate LepR signaling, leptin-dependent metabolism, and feeding-regulating processes. Biochemical experiments, such as co-immunoprecipitation, confirmed the physical link between the channel and the receptor. This interaction is so important that in mice lacking KCNB1, several consequences are observed. Firstly, hypothalamic RNA bulk-sequencing displays an abnormal upregulation of the LepR gene and alterations of other Leptin-signaling molecules. Biochemical experiments demonstrate a robust overproduction of the pro-hormone POMC and consequently the anorexigenic biomolecule, alpha-MSH. Magnetic Resonance Imaging results also show body composition changes (Lean, Fat Mass etc.). Moreover, behavioral tests indicate reduced food intake and abnormal leptin responses. Interestingly, by observing c-FOS changes to

detect neuronal activation, hypothalamic neurons are constitutively dysregulated, anticipating a dual role for KCNB1 in modulating electrical and bio-molecular mechanisms. Based on these findings we can conclude that KCNB1 is a player in energy regulation, ingestive behaviors, and leptin metabolism

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Glucose-Dependent Insulinotropic Polypeptide Receptor Signalling In Oligodendrocytes Increases The Weight Loss Action Of Glp-1R Agonism

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The next-generation of obesity medicines harness the activity of the glucose-dependent insulinotropic polypeptide and glucagon-like peptide 1 receptors (GIPR, GLP-1R), but their mechanism of action remains to be fully elucidated. Here, we report that the GIPR is enriched in oligodendrocytes of the median eminence (ME) and GIPR signalling bidirectionally regulates oligodendrogenesis in the adult ME of diet-induced obese (DIO) mice. In mice with adult-onset deletion of the GIPR in oligodendrocytes, GIPR agonism fails to enhance the weight-loss and appetite-suppressive effects of GLP-1R agonism. Mechanistically, GIPR agonism increases access of GLP-1R agonists to the ME and ARH, and GIPR signaling in oligodendrocyte is required for this effect. Last, we show that vasopressin neurons of the paraventricular hypothalamus are required for the weight loss induced by GLP-1R activation, are targeted by peripherally administered GLP-1R agonists via their axonal compartment in the ME, and this access is increased by GIPR signalling in oligodendrocytes in obese mice. Collectively our findings identify a novel mechanism of action for GLP-1R/GIPR-based weight loss therapies through a GIPR-mediated regulating of the access of GLP-1R agonists to their neuronal substrates for weight loss and support a role for ME oligodendrocyte plasticity in the mechanism of action of incretin-based therapies.

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Hedonic And Homeostatic Neural Correlates During Memory Encoding And Retrieval Of Food Stimuli Relate To Prebiotic Intervention

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Homeostatic and hedonic brain processes shape eating behaviour in concert with the gut-brain axis. Memory functions influence eating behaviour by reinforcing consumption patterns through past experiences, yet the neural correlates of food memory and the influence of gut-brain interactions on memory processes remain underexplored.
This preregistered analysis (osf.io/whbc8/) of a double-blind cross-over randomized clinical trial (NCT03829189), examined neuronal correlates during food versus art memory encoding and retrieval using 3 Tesla task functional MRI in 55 healthy adults (19 females, age 28±6.5, BMI 25-30 kg/m2). We assessed changes following a prebiotic dietary intervention (30g inulin/day for 14 days) versus an isocaloric placebo.
Food memory accuracy was reward-enhanced, eliciting during encoding specific brain regions including nucleus accumbens, pallidum, caudate, cingulate, dorsomedial prefrontal cortex (dmPFC), and ventral tegmental area (VTA), while retrieval additionally activated the hippocampus and amygdala. Food memory encoding further elicited activations in the hypothalamus which were inversely related to ghrelin levels.
Following prebiotic intervention, a decline in neural food memory activations was noted in hedonic areas (dmPFC, orbital frontal, anterior cingulate, caudate, thalamus, VTA), homeostatic areas, and hippocampus. Homeostatic brain activity changes partly correlated with insulin, GLP-1, leptin, and hippocampal activity changes related to gut microbiota abundance changes.
This study indicates that neuronal food-related memory processes are dependent on homeostatic and hedonic brain signals that are modulated by the gut-brain axis. Our findings thus raise implications for the treatment of obesity and substance use research.

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Exercise-Induced Activation Of Ventromedial Hypothalamic Neurons Mediates Improvements In Endurance

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Regular exercise training is one of the most robust and effective lifestyle interventions for improving health. It is known to induce a network of long-lasting peripheral changes to skeletomuscular, cardiovascular, and metabolic systems. The role of the brain in both responding to and driving these changes is not well understood. Here we show in mice that steroidogenic factor-1 (SF1) expressing neurons in the ventromedial hypothalamus (VMH) play a critical role in exercise-mediated changes. SF1 neurons are activated immediately following an exercise session, and this activity increases over time with more training. This increase in post-exercise activity is associated with increases in intrinsic excitability and synaptic plasticity onto SF1 neurons. Inhibiting this activity is sufficient to prevent the normal, training-induced improvements in endurance capacity. Conversely, optogentically amplifying this post-exercise activity drives an additional boost in endurance capacity. Overall, these results demonstrate that exercise-induced hypothalamic SF1 neuron activity is essential for the coordination of physiological improvements from exercise training.

P152 **Long-Acting Glp-1/Amylin Analogue Combination Therapy Spares Mesolimbic Signaling**

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GLP-1 receptor agonists (GLP-1RAs) administered either peripherally or centrally, attenuate food intake and measures of food motivation and reward. Moreover, combination therapies that include GLP-1RAs are increasingly being developed for weight reduction. It remains unclear whether the impact of weight-reducing agents is due, in part, to a direct effect on reward-related dopamine (DA) signaling. Here, we trained ad libitum-fed rats (n=12) for ten days on a Pavlovian conditioning paradigm, where each of five different auditory cues predicted the onset of a unique frequency of brain stimulation reward (BSR). BSR was delivered to the medial forebrain bundle (MFB) through a chronically implanted electrode. Spontaneous DA transients and phasic spikes evoked by cues and stimulation were measured in the nucleus accumbens core (NAC) using the fluorescent sensor GRABDA and fiber photometry. Dopamine responses to cues developed and stabilized over 10 days of training. After training, rats received a daily injection of a combination of the amylin receptor agonist cagrilintide and the GLP-1RA semaglutide (CagriSema) in escalating doses. Treatment dose-dependently reduced body weight. In addition, while it had no effect on cue-evoked DA, there was a dose-dependent decrease in stimulation-evoked DA release. These data suggest that clinically relevant treatments for overweight and obesity can act through, in part, effects on phasic dopamine signaling.

P154 **Time-Restricted Feeding In Adolescent Female Rodents And Susceptibility To Obesity**

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Time-restricted feeding (TRF) is a form of intermittent fasting that limits eating to a short time window and is a clinical approach to treating obesity; however, the safety and efficacy in adolescents remains unknown. We developed a rat model of adolescent TRF to determine impacts on weight gain, body composition, and neurocognitive development. Adolescent female Sprague Dawley rats were divided into four dietary groups: ad libitum standard chow (ad lib chow; n=10) or Western Diet (ad lib HFHS; n=12) (Research Diets D12451), or the same diets with food access restricted to 8 hours per day during the dark cycle (TRF chow, n=12; TRF HFHS, n=12). The Barnes Maze and Elevated Plus Maze were used to measure learning and memory function and anxiety-like behavior, respectively. Data were analyzed using three-way ANOVAs with Holm Sidak post hoc analyses ($P<.05$ considered significant). There was a time x TRF and time x diet interaction with a main effect of TRF and diet, where TRF animals had lower caloric intakes and body weights than ad libitum counterparts and WD-fed animals were heavier than CD-fed animals. TRF animals had lower lean mass than ad libitum-fed animals on a similar diet but gained similar amounts of fat mass. Thus, the differences in body weight were driven by reduced lean mass in animals on TRF. There were no group differences in anxiety-like behavior. TRF chow-fed animals had impaired memory function during adulthood compared to ad libitum controls. TRF during adolescence does not reduce susceptibility to diet-induced fat gain despite lowering body weight and food intake. Further testing is needed to determine how TLF may impact the health of adolescents in whom obesity is already established.

P156 **Control Of Consummatory Behavior By A Lateral Hypothalamus To Paraventricular Thalamus Pathway**

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Obesity is a global health problem often driven by excessive consumption of high-caloric food. The brain plays an important role in food selection, and the lateral hypothalamus (LH) is a critical regulator of food intake. Its GABAergic neurons (LH^{GABA}) send projections to the paraventricular thalamus (PVT). However, the role of this pathway in food intake remains incompletely understood. In this study, we investigated the influence of the LH^{GABA} to PVT pathway on consummatory behavior by inducing the expression of channelrhodopsin-2 (ChR2) in Vgat-cre mice (ChR2: n=8; Control: n=5). Optogenetic activation of the LH^{GABA} to PVT pathway was performed in vivo during the presentation of various taste stimuli while consummatory licking was monitored. Since it is known that activation of the LH^{GABA} evokes consummatory behavior we hypothesized LH^{GABA} to PVT pathway stimulation would have a similar effect. Our results reveal that activating this pathway elicited ingestive behavior in response to sweet and bitter taste stimuli and even an empty sipper empty. This effect was potentiated after mice were given ad libitum access to high-fat diet (HFD) for 3 weeks. To investigate whether HFD alters LH^{GABA} activity, we expressed the calcium sensor GCaMP6 in LH of Vgat-Cre mice (n=4) and recorded neural activity in vivo using two-photon microscopy. Interestingly, we observed reduced LH^{GABA} neuron activity following chronic HFD exposure. These findings suggest that a decrease in neural activity may increase the sensitivity of LH^{GABA} neurons to optogenetic stimulation due to changes in their activation threshold. Our work proposes that the LH^{GABA} to PVT pathway contributes to overconsumption by enhancing sensitivity after prolonged HFD consumption, thereby facilitating overeating.

P158 **Food Insecurity During Development Impairs Memory Function During Adulthood In Male Rats**

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USDA estimates indicate that 13.5% of U.S. households are currently food insecure. The neurobiological effects associated with unpredictable food access during early life periods of development are poorly understood. We devised a novel food insecurity model to control the timing, type, and quantity of accessible food using programmable feeders to investigate the relationship between early-life food insecurity and behavioral outcomes in male rats during adulthood. Rats were divided

into 3 groups (n=15-16/group): Secure-Chow (SC), 1st control group given 100% of caloric needs, distributed evenly across 4 set mealtimes of standard chow daily; Secure-Mixed (SM), 2nd control group given predictable alternating access to either chow or high-fat, high-sugar diet (HFHSD; 45% kcal from fat) at 100% of caloric needs, distributed evenly across 4 set mealtimes daily; and Insecure-Mixed (IM), the experimental group given randomly alternating access to either chow or HFHSD at either 85% or 115% of daily caloric needs, distributed evenly across 4 set mealtimes, with 1 meal randomly skipped daily. These feeding schedules were implemented from postnatal days (PNs) 26-45, and from PN 46 onwards all groups received chow ad libitum. Metabolic and behavioral assessments performed in adulthood (PN 60+) revealed no group differences in food intake, body weight, body composition, or anxiety-like behavior (zero maze and open field procedures). However, the IM group exhibited hippocampal (HPC)-dependent spatial memory impairments compared to the SC and SM control groups in the novel location recognition test. These findings suggest that early-life food insecurity may be associated with long-term impairments in HPC-dependent memory function.

P160 **Ventral Tegmental Area Dopaminergic Neural Activity In Response To Medial Forebrain Bundle Stimulation In An Associative Learning Paradigm**

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Opioids act on the mesolimbic dopamine pathway and chronic exposure has been shown to alter this circuit, with effects on a wide range of motivated behaviors and decision-making. A limitation of many preclinical models of neurocognitive effects of substance abuse is the necessity to modify physiological state of the subject to engage motivated behavior. These manipulations themselves alter signaling in the mesolimbic dopamine system. Brain stimulation reward can bypass this confound by delivering non-contingent stimulation (nBSR) to the medial forebrain bundle (MFB). We developed a Pavlovian cue-stimulation paradigm to examine mesolimbic dopamine activity in response to MFB stimulation using *in-vivo* fiber photometry to probe reward learning and sensitivity. A fiber optic cannula was implanted in the ventral tegmental area (VTA) of Long Evans rats (n=4) and a bipolar stimulating electrode was implanted in the MFB. Each experimental session consisted of presentation of an auditory tone followed by stimulation in the MFB. Five stimulation frequencies were used (0 Hz, 50 Hz, 63 Hz, 79 Hz, 141 Hz) each paired with a unique tone. Each session consisted of 10 blocks with 5 trials, with the cue-stimulation pairing presented in a randomized order. Data were normalized to the pre-trial baseline. Responses to each cue and stimulation were analyzed by trial type. Through training, animals develop consistent responses to each unique cue, demonstrating the sufficient signals to discriminate between cue-stimulation pairings. This paradigm will be used to assess how occasion-setting contexts differentially paired with opioid exposure affects VTA dopamine to nBSR administration, associative learning, and predictive cue responses.

P162 **Environmental Enrichment Exposure Decreases Intrinsic Excitability Of Extended Amygdala Crf+ Neurons And Sex- Specifically Modulates Associated Ethanol Consumption And Anxiety Behaviors In Adolescent Mice**

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Alcohol Use Disorder (AUD) affects 1 in 12 adults and costs the United States over $249 billion annually. Binge ethanol consumption during adolescence is highly predictive of future AUD, a phenomenon that has driven significant interest in understanding the neurobiological vulnerabilities present during this critical period. Specifically, the central CRF system within the extended amygdala is known to modulate anxiety-driven binge drinking behavior in mammals. However, the extent to which adolescent environmental stress influences the development of AUD-linked CRF circuitry remains poorly understood. To investigate this, we conducted a longitudinal behavioral study, exposing C57BL/6J mice to either enriched or impoverished housing conditions during early adolescence (P20–32). We assessed anxiety-related behaviors using the Elevated Zero Maze, Marble Burying, and Novelty Seeking tasks and measured binge drinking using the Drinking in the Dark paradigm. To examine developmental changes in CRF circuitry within the extended amygdala, we performed intrinsic excitability recordings of CRF+ neurons in both the CeA and vBNST in male and female mice. We found that mice from the enriched treatment group exhibited decreased intrinsic excitability in these circuits. In summary, our findings reveal how CRF circuitry development, binge drinking behavior, and anxiety-related phenotypes are shaped by early adolescent environmental conditions. This highlights a critical developmental window and a potential circuit-based target for future preventative AUD therapies.

P164 **Semaglutide (Sema) Acutely Decreases Intake Of Sucrose-Rich Food & Blunts Body Weight Cycling In A Rat Model Of Binge-Eating**

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This study aims to better understand the effects of SEMA on food-seeking behavior and bodyweight (BW) in a rodent model of binge-eating disorder. While the drug's safety and efficacy has been established in humans with type 2 diabetes, its impact on the unique metabolic and behavioral profile that defines compulsive eating is less clear. In this study, we established binge-eating behavior by providing 12 adult female rats with intermittent access to a modular operant conditioning device (FED3) that dispensed sucrose-rich, nutritionally-complete, and highly preferred food pellets (SUC) in response to a nose poke (FR1 schedule of reinforcement). Once rats established reliable binge-like intake, they received SEMA (s.c., escalating doses) or vehicle injections twice weekly, with SUC-access sessions either immediately or 24 hours after injection. BW before and after SUC access sessions, as well as pellets earned, were recorded across each 7h session. SEMA eliminated the expected BW-cycling compared to controls at all doses tested. SEMA also robustly reduced total SUC intake in sessions immediately following injection, and hourly intake assessments showed a sustained, or even increased hypophagic effect over the course of these 7h sessions. When SUC access began 24 hours after drug administration, total intake was only reduced in sessions associated with a recently escalated dose of SEMA, likely reflecting a dose-related sensitization. Results suggest a role of GLP-1 systems in modulating the reward value of palatable food within the unique behavioral context that defines compulsive eating. Given its fast-acting and robust behavioral effects at low doses demonstrated here, it may have clinical promise in treating compulsive/binge eating-associated eating disorders.

P166 **Mediobasal Hypothalamic Aryl Hydrocarbon Receptor Is Critical For Metabolic Homeostasis Via Regulation Of Hypothalamic Inflammation.**

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The gut microbiota saliently contributes to host metabolic health, partially via generating metabolites from dietary components. Indoles are bacterial metabolites of dietary tryptophan that can reduce central inflammation through aryl hydrocarbon receptor (AhR) signaling. Western Diet (WD)-feeding rapidly induces mediobasal hypothalamic (MBH) inflammation and reduces gut indole levels compared to chow-fed controls. However, the link between indoles and WD-induced MBH inflammation has not been investigated. We hypothesize that reductions in hypothalamic indole-AhR signaling drive WD-induced hypothalamic inflammation and obesity. First, we knocked down AhR in the MBH of chow and WD-fed mice; AhR knockdown drastically increased impaired energy and glucose homeostasis in both groups. After 10 weeks, AhR knockdown chow-fed mice had body weight and adiposity levels matching 10-week WD-fed obese mice. Immunofluorescence and RNAscope analyses of the MBH revealed increased astrogliosis and inflammatory cytokine expression in AhR knockdown groups. Next, we knocked down AhR in either neurons or astrocytes in the MBH. AhR knockdown in astrocytes and neurons impaired energy and glucose homeostasis, although not to the level of the total knockdown. Dual knockdown of AhR in both neurons and astrocytes in the MBH recapitulates the impairment in energy and glucose homeostasis seen with the ubiquitous MBH AhR knockdown. Lastly, we found that 3rd ventricle infusion of AhR agonists could reverse WD-induced obesity via reductions in food intake. Together, these data demonstrate that MBH AhR signaling is critical for metabolic homeostasis and that WD-induced reductions in indole-AhR signaling may drive obesity, highlighting MBH-AhR signaling as a promising therapeutic target for obesity.

P168 **Cgrp Signaling In The Locus Coeruleus Suppresses Food Intake Without Inducing Gastrointestinal Malaise Or Aversive State Changes**

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The locus coeruleus (LC) is a conserved brainstem nucleus recently identified as a key regulator of feeding behavior through neuropeptide signaling. While calcitonin gene-related peptide (CGRP) is well known for its role in migraine pathology and appetite regulation via hindbrain regions like the parabrachial nucleus, the function of LC CGRP receptor signaling related to feeding behavior remains unexplored. Given the LC's involvement in arousal and autonomic responses, it is unclear whether CGRP signaling in this region influences feeding independently of aversive effects. Specifically, we sought to investigate whether CGRP in the LC can suppress food intake without inducing significant aversive-like behaviors. Here, rats receiving microinjections of CGRP into the LC show that CGRP receptor activation in the LC suppresses food intake and body weight by decreasing meal frequency. Moreover, this suppression of food intake is not driven by gastrointestinal malaise (pica behavior), altered pain sensitivity (hot plate test), or anxiety-like behaviors (open-field test). Furthermore, our RNAscope and pharmacology data suggest that CGRP signaling primarily acts through calcitonin receptor complexes in the LC. Our work establishes the LC as a critical site of action for CGRP signaling and provides new insights into the endogenous mechanisms by which CGRP regulates feeding behavior. Funding: NIH: NIDDK105155 and K01DK133627.

P170 **The Effect Of Photoperiod And Temperature On Growth And Energy Balance In Tundra Voles (Alexandromys Oeconomus)**

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Photoperiod and temperature are crucial environmental cues that enable seasonal adaptations in small mammals. While photoperiodic regulation of reproduction is well-studied, its interaction with temperature in shaping growth and energy balance remains unclear. This study investigates how photoperiod and temperature interact to influence growth and energy regulation in Tundra voles. We hypothesize that voles in a long photoperiod (LP) exhibit higher body mass than those in a short photoperiod (SP) and that lower temperatures enhance this effect. We studied 187 voles born under LP (16L:8D) or SP (8L:16D) at 21 ± 1C until weaning. On day 21, they were transferred to temperature-controlled rooms (21 ± 1C or 10 ± 1C) under either SP (autumn program) or LP (spring program). Body mass, organ weights, body composition, activity, food intake, digestion efficiency, total energy expenditure, and relevant gene expression were measured at specific ages. Data were analyzed using a general linear model (GLM). Our results show that the voles in the spring program had higher body mass and activity levels under the influence of photoperiod, accompanied by increased food intake, digestion efficiency, and total energy expenditure compared to the autumn group. Temperature significantly influenced food intake, while its impact on other measured variables emerged later. These findings highlight the complex interaction between photoperiod and temperature in regulating seasonal energy balance, providing insight into metabolic adaptations in small mammals.

P172 **Role Of Hypothalamic Agrp Neurons In The Control Of Glucagon Secretion By Amylin**

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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.While the mechanism by which amylin inhibits glucagon secretion remains largely unexplored, evidence suggests that the brain may be involved. 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 and mouse 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 and that a subset of ARC neurons co-express *AgRP*, *CTR* and *RAMPs* at the cellular level. Our data highlight that CTR and RAMP2 mRNA expression does not vary significantly along the anterior-posterior axis of the ARC and that nearly 50% of AgRP neurons co-express CTR and RAMPs. Furthermore, we are refining a model to investigate amylin's glucagonostatic action and our first tests demonstrated that amylin consistently reduced L-arginine-induced glucagon secretion in freely-

moving rodents. Further refinement will allow us to 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.

P174 **Effects Of A Moderate Reduction In Plant Protein Intake On Feeding Behaviour In Rats.**

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Effects of a moderate reduction in plant protein intake on feeding behaviour in rats. Context: Reducing animal protein intake and shifting towards more plant-based protein sources in Western societies is recommended to decrease the environmental impact of the food systems. Reducing dietary protein increases caloric intake and adiposity in rats fed animal protein-based diets as predicted by the protein leverage framework. This study aims to test protein leverage in the context of plant-based diets. **Methods:** 6-week-old male Wistar rats were divided into 7 groups of 8 animals each. 2 groups were fed a diet with 6% or 20% of energy as animal protein (casein) and 4 groups were fed a plant protein diet (wheat+lentils) at 8, 10, 13, 15 and 20% for 10 weeks. Caloric intake, body composition, circulating FGF21 and ghrelin levels and hepatic expression of IGF1 were measured as markers of protein and satiety status. Preference for fat and sugar was measured in a food-choice test. **Results:** Rats fed the 6% animal-based diet consumed more food than rats fed 20% diets ($p<0.01$) and had higher visceral adiposity ($p<0.01$) with no difference in body weight. Rats fed plant-based diets displayed a progressively impaired growth ($p<0.01$), except at 20% protein, with no increase in food intake. Low-protein diets, both animal- and plant-based, led to increased plasma levels of FGF21 and hepatic IGF1 ($p<0.01$), increased ghrelin ($p=0.011$) and preference for fat-sugar. **Conclusions:** Plant-based diets with a moderate reduction in protein do not lead to increased food intake to compensate for the protein reduction and thus impair growth in young rats. The absence of increased food intake could be explained by a nutritional stress induced by the low protein status. This was assessed by hypothalamic expression of CRF (Corticotropin Releasing Factor) increased in rats fed the low plant-based protein diet ($p=0,03$ ANOVA) which could lead through cortisol release to inhibition of food intake. A second explanation could be linked to the quantity of short chained fatty acids (SCFA), such as butyrate and propionate, in the gut of rats fed the plant-based protein diet which were higher than low animal-based protein group ($p=0,045$) and at the same level as rats fed the normal animal-based protein diet. These SCFA can bind free fatty acids receptors (FFAR) of gut cells stimulating GLP-1 release to increase satiety. Otherwise, a moderate reduction in protein from animal- and plant-based diets did increase appetite for palatable food which could be explained by increased ghrelin plasmatic levels as a motivator for reward-based eating.

P176 **Oleoylethanolamide As A Cardioprotective Agent Against Diet-Induced Fibrosis And Metabolic Impairments**

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The potential role of the signal molecule, protein kinase B (Akt), and the energy fuel AMP-dependent protein kinase (AMPK) has been highlighted in obesity-induced cardiac metabolic changes. In this scenario, a central role for peroxisome-proliferator activated receptor (PPAR)-α has been addressed in preserving cardiac function during metabolic insult. Here, we investigated the possible cardioprotective effect of the PPAR-alpha agonist, oleoylethanolamide (OEA), in a rat model of overweight. To meet this aim, adolescent male Wistar rats were fed a high-fat diet or a low-fat diet for 7 weeks; both groups were treated for 2 weeks either with vehicle (saline/polyethylene glycol/Tween 80) or OEA (10 mg/kg, intraperitoneally). After treatment rats were sacrificed and hearts were processed to assess histological changes, transcriptomic differences in genes involved in fibrosis, Akt/AMPK expression, lipid metabolism and mitochondria bioenergetics by using thin layer chromatography, PCR and western blot analysis. Data were statistically analyzed by using two-way ANOVA with Tukey as a post-hoc test. In overweight rats, OEA treatment reduced food intake and body weight gain. Moreover, overweight rats showed: cardiac fibrosis further confirmed by altered expression of fibrotic genes; a reduced AMPK (energy sensor) and an increased Akt (energy promoter) signaling. Interestingly, such alterations were restored by the pharmacological treatment with OEA. No differences were observed in lipid metabolism and mitochondria bioenergetics. Although preliminary, these findings support the hypothesis that activation of PPAR-α by OEA may represent a valid therapeutic strategy to counteract cardiac dysfunctions associated with overweight, by modulating key metabolic and fibrotic pathways.

P178 **Impact Of Current Breeding Practices On The Health And Wellbeing Of The Mouse Dam**

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In the EU, around 50% of experimental animals are mice, totaling over 4 million used in 2022. We assume these mice were born from healthy female breeders, yet we have little data to support this. Current breeding practices are designed to maximize breeding productivity, exposing the dam to the physiological stress of concurrent pregnancy and lactation – but the effect on her welfare is unknown. This exploratory analysis investigates whether breeding experience impacts the health of the mouse dam. Two inbred mouse strains [C57BL/6J; BALB/cByJ] were used to assess behavioral, metabolic, and nutritional endpoints in postpartum dams. The effect of the number of breeding cycles [1, 2, or 4] and the lactation duration [3 or 4 weeks] was investigated, and animals were compared to age-matched non-breeding females [virgins] [N = 5-10 / group]. Linear mixed effect models demonstrate that maternal body weight during lactation increases with the number of reproductive cycles. Indirect calorimetry showed that neither parity nor weaning time impacted respiratory exchange ratio, while energy expenditure was decreased in two-time pregnant dams and virgin animals compared to one-time pregnant dams. Oral glucose tolerance tests two weeks after weaning revealed an improved glucose tolerance in reproducing females in the C57BL/6 strain, while insulin sensitivity was only affected by strain and not parity or weaning time. Lastly, pregnancy led to changes in bone mineral density still detectable five weeks after weaning, while lactation duration had no effect. In

conclusion, while repeated pregnancy cycles led to measurable physiological changes in breeding mouse dams, we found no clear evidence of substantial health impairment after four consecutive rounds of pregnancy and lactation.

P180 **Hepatocyte Gaba Transaminase Knockdown Does Not Affect Glucose Homeostasis, Food Intake, Or Body Weight**

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Rationale: Obesity induced liver lipid accumulation increases liver GABA synthesis and release. Liver GABA is produced when succinate enters the GABA shunt, a pathway with two enzymes, succinate semialdehyde dehydrogenase and GABA transaminase (GABA-T). Peripheral GABA-T inhibition or antisense oligonucleotide mediated knockdown improves insulin sensitivity and glucose tolerance and decreases food intake, body weight, basal serum insulin, and *ex vivo* liver slice GABA release in diet-induced obese mice.**Hypothesis:** Hepatocyte-specific knockdown of GABA-T will decrease liver GABA synthesis, improving metabolic homeostasis in diet-induced obese animals.**Species, Subjects, and Procedures:** We performed two studies to assess the effect of hepatocyte specific GABA-T knockdown. Knockdown was initiated by tail-vein administration of an AAV9-TBG-Cre ($1X10^{11}$ genome copies) into mice that were homozygous for either the wildtype GABA-T allele or a loxp flanked GABA-T allele. In our first study, we initiated the knockdown in diet-induced obese mice (n=12). In our second study, we initiated the knockdown in lean mice (n=16) and assessed glucose homeostasis and body weight at 0, 3, 6, and 9 weeks on high fat diet (Envigo TD.06414).**Results:** AAV delivery resulted in a >75% decrease in liver GABA-T mRNA expression in mice homozygous for the floxed allele relative to mice with two wildtype alleles. Independent of the timing of AAV delivery relative to the onset of diet-induced obesity, knockdown of hepatocyte GABA-T expression did not affect glucose tolerance, insulin tolerance, serum insulin, body weight, or liver slice GABA release.**Conclusion:** GABA is not produced by hepatocytes. Identifying the cell type responsible for liver GABA production will aid in targeted therapeutic development.

P182 **Investigating Lipid Sensing In Human Cck-Secreting Duodenal I-Cells**

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Cholecystokinin(CCK), a gut hormone secreted from the small intestine in response to food intake, relays signals of nutrient intake to the brain through vagal afferents, inhibiting further food intake, whilst also enhancing the preference for nutritious sweet and fatty foods. However, the molecular mechanisms by which luminal contents stimulate CCK secretion have been incompletely elucidated, primarily due to the difficulty in distinguishing I-cells from other intestinal epithelial cells. This study aims to evaluate the molecular mechanisms involved in the regulation of CCK secretion in human intestinal organoids in response to lipids. CRISPR-Cas9 was used to generate human duodenal organoids with fluorescently labelled I-cells. CCK-Venus organoids enabled RNA-sequencing of fluorescently-assisted sorted I-cells revealing high expression of receptors for long- (FFAR1, FFAR4) and short-chain (FFAR2) fatty acids, and mono-acylglycerols (GRP119), as well as bile acids (GPBAR). Loading CCK-Venus cells with Fura-2 enabled monitoring of single cell Ca^{2+} dynamics, revealing clear responses to different chain-length fatty acids (acetate, butyrate, decanoate, laurate, eicosapentaenoate and oleate) and the FFAR1 agonist AM1638 (n>5/stimulus). Live single-cell imaging, performed in human CCK-EpacS-H187 organoids, expressing a fluorescent cAMP-indicator,showed cAMP increases in response to agonists of GPBAR1 and GRP119 (n>5/stimulus). Secretion studies confirmed CCK release in response to selective agonists of FFAR1, GPBAR and GPR119, but not FFAR4. Generation of receptor knock-out organoids are in progress to evaluate the relative importance of these receptors/molecular mechanisms for CCK release in response to lipid stimuli and results are hoped to be included at the meeting.

P184 **Naturalistic Functional Neuroimaging Of Food Reward In Anorexia Nervosa**

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Anorexia nervosa (AN) is a serious psychiatric condition, in which restrictive eating leads to health-harming weight loss. Persistent energy restriction in AN may reflect alterations in the neural circuits that encode food reward. However, traditional behavioural assays of reward-related cognition lack ecological validity, and naturalistic paradigms (e.g., movies) address this limitation by evoking complex cognition in contexts that reflect one's daily life. Here, we tested if movie-watching can improve detection of altered brain connectivity patterns in women with AN. Women with AN were hypothesised to have altered functional connectivity (FC) of medial frontal, limbic, and default mode networks relative to controls, which would be further increased in response to naturalistic stimuli. Women with AN (n=24) and healthy women (n=27) underwent functional MRI scanning, during which they performed an instrumental learning task and watched two movies, depicting either food or social reward. After preprocessing functional data in AFNI, we generated connectomes for each functional run per participant using the 268-node Shen atlas. Group differences in FC across 10 canonical brain networks were examined using constrained Network-Based Statistics (one-tailed, alpha=.025, K=5000 permutations). Preliminary results indicated that FC of medial frontal, default mode, and visual networks differed significantly between groups during the decision-making task; however, we did not observe group differences in network-level FC during movie-watching. Within the AN group, frontoparietal, default mode, and visual network FC differed between the food movie and decision-making task. These findings provide initial support for the use of naturalistic paradigms to delineate the neural mechanisms of AN.

6:30 - 8:00 PM	Offsite - The King's Arms Oxford
New Investigator Event, organized by the New Investigator Advisory Committee	

NOTE: We have reached capacity. Thank you all for signing up! If you plan on walking over from the conference with the group, please look for Laura Loera-Lopez, Lauren Raycraft, Rachel Donka, and Nick Neuald - they will be guiding everyone to Kings Arms! See you all there!Come meet your fellow new investigators.

Wednesday, July 30, 2025

8:00 - 4:00 PM	Registration - South Mezzanine
Registration	

9:00 - 10:00 AM	South Mezzanine
Poster Session 3, Exhibits & Coffee Break	

P203 **Differentiation Of Positive And Negative Emotional Eating: Internal And External Factors**

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Positive (PEE) and negative emotional eating (NEE) have unique relationships with eating problems and BMI. We explored whether PEE and NEE would differ in relation to externalized (e.g., external eating, busyness) and internalized (e.g., irrational beliefs, impulsiveness, anxiety, depression) factors in 241 students. Significant, small correlations were found for NEE and lack of premeditation (LoP; r=-.15), positive urgency (PU; r=.13), self-downing (r=.14), and external eating (ExE; r=.17). Significant correlations were found for PEE and self-downing (r=-.14) and ExE (r=.17). Hotelling's t-tests showed that there was a significant difference between the correlations for LoP and NEE and PEE (r=.10), $t(238)$=-2.53, p=.01, and for self-downing, $t(238)$=2.83, p=.01. Thus, internal factors may be more strongly associated with NEE than PEE. Regressions examined which internal and external variables (with significant bivariate associations) were unique correlates of NEE (external factors entered first, then internal) and PEE (factor order reversed). Only ExE was a unique correlate of NEE, B=.14, p=.02. For PEE, self-downing was linked to lower PEE scores, B=-.17, p=.02, which remained when BMI (covariate) and ExE were added. Like NEE, ExE was linked to elevated PEE, B=.17, p=.01. Moderation analysis revealed that in those 1 SD below the mean for BMI, ExE was more strongly and positively linked to NEE as ExE values increased. For PEE, main effects showed significant associations with ExE, irrespective of BMI. As expected, PEE was lower when self-downing was higher and when ExE was low. ExE may be a more powerful cue for NEE in people with lower BMI whereas people in larger bodies may be more impacted by internal processes (e.g., emotional regulation difficulties; disordered eating).

P205 **The Addiction-Susceptibility Polymorphism Taqia/Ankk1: Role In Reward- And Metabolic-Associated Disorders.**

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TaqIA is a single nucleotide polymorphism located in the Annk1 gene, leading to two alleles, A1 and A2. Approximatively 30% of the world population have one or two copies of the A1 allele. The presence of this allele increases the likelihood of developing neurological and psychiatric disorders, as well as an increased risk of obesity, indicating a role for this gene in energy homeostasis. While the A1 allele is the ancestral variant, the derived A2 variant has appeared with the Homo taxon, impeding the understanding of its causal role in neuropsychiatric and metabolic disorders. We have then generated a single point mutation to humanise mice for the A2 allele. Motivation of male and female mice of both A1/A1 and A2/A2 genetic backgrounds was assessed in operant cages where reward is a 30s-access to feeders filled with food. Females A2/A2 mice significantly increased their number of active presses in a Fixed-Ratio 1 paradigm compared to their A1/A1 counterparts. However, this effect is lost when the cost to get the reward is higher or when the reward is more palatable. Males A2/A2 significantly increased their number of feeders visits compared to their A1/A1 counterparts. This phenotype is heightened where the reward is more palatable, and lost when the cost to get the reward is higher. Metabolism of male mice of both A1/A1 and A2/A2 genetic backgrounds was also assessed in indirect calorimetry cages. Interestingly, only males A2/A2 displayed higher energy expenditure under both chow and habituation to a high-fat diet conditions than their A1/A1 counterparts. Altogether, these data confirm the importance of the role of the TaqIA polymorphism in the regulation of reward-related behaviours and energy homeostasis, and underscore a sexual dimorphism in these contexts.

P207 **Vagal Remodeling In Early Obesity Disrupts Gut-Brain Signaling But Satiety Is Restored By Activating Downstream Neurons**

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Vagal sensory neurons integrate meal-related signals to control food intake, but their function is disrupted in obesity. When this dysfunction emerges and how it affects feeding control remain unclear. We hypothesize vagal dysfunction drives obesity onset. **Results:** Within three weeks of high-fat feeding, anatomical mapping reveals a striking retraction of gut-innervating

vagal fibers in the nucleus tractus solitarius (NTS) (n=6/group, p=**), accompanied by a reduced ability of vagal stimulation to suppress food intake (n=8/group, ns). This trend is seen in both mice and rats. By eight weeks, vagal fibers reinnervate the NTS but target a distinct neuronal population, suggesting a remodeling process that alters gut-brain communication (n=5/group, p=**). Despite this reinnervation, two-photon calcium imaging of vagal sensory neurons reveals persistent deficits in responsiveness to gastrointestinal stimuli, including gastric distension, indicating that both structural and sensory impairments contribute to gut-brain dysfunction (n=4/group, p=***). Notably, chemogenetic stimulation of lean-state meal-responsive NTS neurons suppresses feeding even in obesity, demonstrating that downstream circuits remain functional despite diminished vagal input (n=8/group, p=***). However, activation of the newly recruited NTS neurons in obesity leads to an even greater suppression of food intake, despite their reduced activation by meals (n=8/group, p=***). **Conclusion:** This suggests that while these neurons receive weaker vagal input, they retain the capacity to strongly modulate feeding when engaged. These findings establish vagal remodeling as a key driver of obesity-related gut-brain dysfunction and reveal an alternative NTS neuronal population with heightened satiety-inducing potential.

P209 **Neural Fmri Responses To Food Combinations In The Human Brain**

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Modern eating typically involves combinations of interacting foods rather than isolated items. For example, cake paired with coffee is more enjoyable than either consumed alone. Such foods complement each other. Conversely, substitute foods (coffee/tea) satisfy similar needs, where having one reduces desire for the other. Here, we investigate these food relations behaviourally and neurally. Thirty-eight healthy human volunteers (22 women; BMI range = 18.8–26.5) underwent fMRI while evaluating (through willingness-to-pay, WTP) for paired or individual foods. Consistent with previous findings, fMRI results showed that the ventromedial prefrontal cortex (VMPFC) encodes food values (MNI = -4, 38, 2; $p < 0.05$, FWE-corrected). Behaviourally, value differences between paired and individual foods increased for complementary foods and decreased for substitute foods. Additionally, Bayesian hierarchical regression, showed that the frequency of co-consumption increased complementarity whereas nutrient similarity decreased it. To interrogate the neural bases of the different food relationships, we conducted a representational similarity analysis on the fMRI data. Specifically, we tested which brain regions represent complementary foods more similarly than substitute foods and vice versa. We find that complementary relations are associated with higher similarity in ventromedial prefrontal cortex (MNI = -6,40,2; $p<0.001$, uncorrected). By contrast, substitute foods are represented more similarly in parietal cortex (MNI=-28 -48 50; $p<0.001$, uncorrected). Together, our behavioural and neural findings suggest that similarity between foods can affect how people value food combinations, paving the way for interventions aimed at promoting balanced and nutritious eating habits.

P211 **Adolescent Morphine Exposure Reduces Vta Da Excitability And Amplifies Adulthood Re-Exposure Effects On Da Signaling**

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Adolescent opioid abuse significantly increases the long-term risk of substance use disorder. Prior work in our lab utilized rate-frequency intracranial self-stimulation (ICSS) to assay the effects of adolescent morphine administration and adulthood re-exposure in Long-Evans rats (n=26). Adolescent morphine administration increased ICSS sensitivity, but withdrawal resulted in a significant and prolonged reduction. In adulthood, prior adolescent morphine exposure led to greater increases in sensitivity during administration, but exacerbated decreases after discontinuation. To determine if adolescent morphine withdrawal altered neurophysiological properties of VTA dopamine (DA) cells, we performed whole cell patch clamp recordings (n=12; TH:Cre^{+}) in morphine and control treated rats following injection discontinuation (PD52-55). Adolescent morphine treatment resulted in reduced electrophysiological excitability of VTA DA neurons. Finally, to examine DA release in vivo, we used fiber photometry to record DA dynamics in the NAc (dLight1.3b) during adulthood morphine administration and withdrawal. Adolescent rats (n=12) underwent morphine (5mg/kg) or saline treatment (PD45-51) and were surgically prepared with fiber optic cannulae (NAcLS) and stimulating electrodes (MFB) at PD60-61. Recordings during and after adulthood chronic morphine administration revealed increased spontaneous DA transients and DA release to ICSS during administration, but greater DA suppression after discontinuation. In sum, adolescent morphine induces long-term alterations in reward sensitivity and DA activity, potentially increases susceptibility to maladaptive behaviors in adulthood. Further research will explore mechanisms underlying these shifts and potential interventions.

P213 **Glucose-Dependent Insulinotropic Receptor Expressing Neurons In The Area Postrema And Nucleus Of The Solitary Tract Receive Distinct Peripheral Input And Differentially Affect Food Intake**

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Central glucose-dependent insulinotropic polypeptide (GIP) receptor (GIPR) expression is necessary for the weight lowering effects of dual incretin agonists. Studies comparing the neurocircuitries engaged by *Gipr* cells in different brain regions highlight the heterogeneity of the GIPR signaling axis and the need to better define and dissect them.This study investigated how *Gipr* neurons in distinct areas of the brainstem are networked and how they may leverage distinct mechanisms to affect feeding in mice. The effects of chemogenetic activation of *Gipr* neurons in either the area postrema (AP) or nucleus of the

solitary tract (NTS) on meal patterning were compared using FED3 devices, uncovering that these neurons differentially regulate satiation. To characterize the regulatory inputs to *Gipr* brainstem neurons, rabies-assisted monosynaptic tracing was performed. These data revealed that *Gipr*^{AP} and *Gipr*^{NTS} neurons receive dense peripheral inputs from transcriptomically distinct vagal afferent neurons (VANs). Whilst GPR65 expressing VANs primarily input to *Gipr*^{AP}, oxytocin receptor expressing VANs input to *Gipr*^{NTS} cells. These markers correspond to chemosensory versus mechanosensory VANs respectively suggesting that *Gipr*^{AP} and *Gipr*^{NTS} neurons may be engaged by distinct post-ingestive gut signalling. Centrally, *Gipr*^{NTS} neurons receive inputs from the paraventricular nucleus of the hypothalamus (PVH), the bed nucleus of the stria terminalis (BNST), the central amygdala and the posterior subthalamic nucleus. *Gipr*^{AP}neurons receive comparatively fewer inputs from the PVH, BNST, but also from the retrochiamatic nucleus and the pontine nucleus. The role and characteristics of these circuits under different physiological perturbations are currently being assessed.

P215 **Synphilin-1 Induces Obesity-Linked Cognitive Impairments In Mice**

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Synphilin-1 (SP-1) is a cytoplasmic protein with enriched expression in neurons. Previous studies have shown that SP-1 transgenic mice display hyperphagia and obesity. In this study, we investigated whether SP1-induced obesity results in cognitive impairments testing the transgenic mice at 3 months, 10 months, and 20 months of age. We measured behavior using an Open Field Test, the Novel Object Recognition Test, and two separate Y-Maze Tests. We found that there was a significant decrease in locomotor activity and cognitive impairment in SP-1 mice at 10 months of age compared with non-transgenic control mice. At 20 months of age, SP-1 mice displayed severe loss of locomotor activity and a major cognitive impairments. In contrast, at 3 months of age (starting point for the obesity phenotype), there was no change in locomotor activity and performance in cognitive testing was normal compared with results in control mice. These results indicate that SP-1-linked chronic increase in food intake and body weight induces ,may be responsible for the cognitive impairments. Our studies provide novel insights into the understanding of obesity-related cognitive impairment and provide a useful model for future pathogenesis and therapeutic studies.

P217 **Cell-Type Unbiased Characterisation Of Brainstem Neuronal Populations Recruited By Semaglutide**

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The GLP-1 receptor agonist (GLP-1RA) semaglutide has transformed obesity pharmacotherapy, but nausea and other side effects limit adherence and efficacy. Whether semaglutide-induced satiation, satiety, and nausea are mediated by distinct and selectively druggable neural circuits is a crucial but methodologically challenging question. Studies using *Glp1r*-Cre mice have posited the area postrema (AP) and nucleus tractus solitarius (NTS) as key loci for the aversive and/or anorectic effects of semaglutide. However, data from ourselves and others show that GLP-1RAs only recruit a subset of brainstem GLP-1R neurons, plus unidentified non-GLP-1R populations, suggesting cell-type specific approaches may be suboptimal. We therefore used the Targeted Recombination in Active Populations (*TRAP2*) transgenic mouse to develop the 'sema-TRAP' model, to characterise and selectively manipulate semaglutide-recruited neurons. We confirm semaglutide TRAPs significantly more neurons in the AP and NTS than a saline control stimulus, and multiplex *in situ* hybridization reveals that semaglutide preferentially recruits a *Glp1r* and *Prlhr* co-expressing subpopulation, and a non-*Glp1r* neuron population. High resolution metabolic phenotyping of semaglutide-treated mice showed robust effects on meal number, frequency, and termination. To try to disentangle the circuits driving these phenotypic components, we conducted a proof-of-concept chemogenetic activation study, using hM3Dq specifically expressed in sema-TRAP neurons in the AP. Selective reactivation of this sema-TRAP population is sufficient to supress food intake and body weight, confirming the utility of this model for cell-type unbiased molecular and functional characterisation of brainstem neurocircuits recruited by semaglutide.

P219 **Gip Receptor Agonism In The Ventral Hippocampus Reduces Food Intake And Impulsivity**

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Dual agonists targeting glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP) signaling are associated with greater weight loss and reduced side effects when compared to single GLP-1 agonist drugs, yet the neural mechanisms through which GIP enhances efficacy remain to be determined. Here, we evaluated whether the hippocampus (HPC) is a site of action for the effects of GIP signaling on eating and food-motivated behaviors. First, expression of GIP receptors was confirmed in rats in both the dorsal and ventral HPC subregions via fluorescent in situ hybridization, with higher expression in the ventral HPC. Next, adult male rats were implanted with an indwelling canula into the dorsal or ventral region of the HPC and housed in an automated food monitoring cage system. Relative to vehicle treatment, infusion of a GIP receptor agonist in the ventral HPC decreased food intake over a 24-hr period, with a trend towards decreased average meal size. GIP-R agonism in the dorsal HPC, however, had no effect on food intake. As recent research suggests that dual agonists may also be associated with reduced impulsivity, and that the ventral HPC plays a role in impulse control, a second cohort of rats were trained in the differential reinforcement of low rates of responding (DRL) test of impulsive action, where they learn to wait 20s between lever presses to obtain a palatable food reward. Results reveal that ventral HPC GIP-R agonism prior to testing increased efficiency in DRL relative to vehicle treatment, with a higher percentage of non-impulsive vs. impulsive responses. Taken together, these results suggest that GIP-R agonism in the ventral HPC may play an important role in regulating food intake and impulsive responding for palatable foods.

P221 **Sugar, Stress, And The Brain: Unraveling The Links Between High Sugar Intake, Depression, And Blood-Brain Barrier Dysfunction In Rats**

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Overconsumption of sugar can lead to health issues, including Prediabetes, which can develop into Diabetes Mellitus (DM). DM increases the risk of Major Depressive Disorder (MDD) and Blood-Brain Barrier (BBB) disruption, which can contribute to neurodegeneration. In our study, we explored the impact of overconsumption of sugar (a model of Prediabetes) in wild-type Wistar (WT) and Wistar Kyoto (WKY) rats, a genetic model of depression. We hypothesized that overconsumption of sugar water would lead to MDD-like symptoms and BBB disruption. Adult male and female WT and WKY rats (N=48 per strain) received either sugar water (35% sucrose), or regular drinking water for a period of 9 weeks. At 23 weeks of age, we performed a series of behavioral tests to explore depression- and anxiety-like behavior, and cognitive function. Following this, brain MRIs were performed to examine BBB integrity, and Proteomics analysis was performed in the hippocampus to explore protein changes due to increased sugar consumption. The results showed that within WT rats, males and females of the sugar-ingesting group showed more anxiety-and depression-like behavior when compared to the other groups. No cognitive differences were found. Within WKY rats, no significant differences were found within any behavioral tests. MRI data showed that rats who consumed sugar water of both strains had increased BBB leakiness when compared to healthy controls. Proteomics analysis revealed various changes of proteins related to metabolic imbalances, neurodegeneration, and BBB integrity. These findings highlight the ways in which increased sugar consumption can lead to physiological, psychological, and neurological deficiencies.

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Melanin ConcenTrating HorMone Effects On EThanol INtake In Female Rats: Sites Of Action

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Melanin concentrating hormone (MCH) is a neuropeptide produced in the lateral hypothalamus (LH) and zona incerta (ZI) that increases intake of both food and drugs of abuse. In male rats, pharmacological injection of MCH has been shown to increase ethanol intake when injected into the third ventricle, however the effects of MCH on ethanol intake in females remains unknown, as does the impact of activating the MCH neurons themselves. We first hypothesize that MCH neuronal activation modulates ethanol intake in females. Female rats were injected with an AAV2 viral vector containing hm3DGq under the control of the pmch promoter. Our results show that chemogenetic activation of MCH neurons increases intake of a 10% ethanol solution in female rats. We further investigated site-specific activation of MCH1R receptor on alcohol consumption in females in regions related to alcohol intake and motivated responding for alcohol. Female Wistar rats were injected within the central nucleus of the amygdala (ceA; n=13) or nucleus accumbens shell (AcbSh; n=14) with vehicle,0.5,or 1μg of MCH at the onset of the dark cycle in a within-subjects design and intake of ethanol was measured. Results show that CeA infusion reduced 10% alcohol intake at the low dose and had no effect at the higher dose. Estrous cycle had no statistically significant impact on intake. Surprisingly, AcbSh infusion of MCH had no effect on alcohol or water intake at either dose. Taken together, our findings show that activation of MCH neurons increases ethanol intake, but that MCH1R activation in the CeA and AcbSh does not increase ethanol intake. Given that prior research has shown that MCH in the AcbSh increases ethanol intake in males, these data suggest likely sex differences in MCH effects on alcohol intake.

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Dissociable Contributions Of Rostral And Caudal Ventral Pallidum Gaba Neurons To &Lsquo;Liking&Rsquo; And &Lsquo;Wanting&Rsquo; For Sweet Reward.

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The ventral pallidum is a key node that controls 'liking' and 'wanting' components of reward. Within this brain region, mu-opioid and orexin receptor agonists increase positive 'liking' reactions elicited by oral infusions of sucrose in rats. However, the VP neuron subtypes that contribute to 'wanting' vs. 'liking' are unknown. We used optogenetic tools in transgenic GAD-Cre rats to probe VP^{GABA} neuron contributions to 'liking' and 'wanting'. We report that stimulation of VP^{GABA} neurons in posterior VP doubled hedonic 'liking' reactions to sucrose (p <0.001, n = 15, 2-way ANOVA), while rostral VP^{GABA} neurons suppressed 'liking' (p <0.001, n = 11; 2-way ANOVA). While 'liking' was oppositely controlled by the rostral vs. caudal VP^{GABA} neurons, 'wanting' effects were observed uniformly across these sites. Optogenetic excitation of both rostral (p <0.001, n = 19, 2-way ANOVA), and caudal VP^{GABA} neurons increased instrumental lever pressing for sucrose (p <0.001, n = 19, 2-way ANOVA), and food intake (p<0.01, n =7, paired t-test). Finally, we asked if VP^{GABA} neuron stimulation could transform a painful electric shock to become 'wanted' by pairing anterior or posterior VP^{GABA} neuron stimulation with voluntary contacts to an electrified shock rod. Strikingly, optogenetic stimulation of anterior VP^{GABA} neurons resulted in increased contact with the shock rod (p <0.001, n = 10, 2-way ANOVA), demonstrating that these neurons generate attraction to a painful stimulus. By comparison, stimulation of caudal VP^{GABA} neurons failed to produce 'wanting' for the rod, further highlighting a functional dissociation between 'wanting' vs. 'liking' in VP. Our results support a critical role for VP^{GABA} neurons in the control of 'liking' and 'wanting'.

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Unravelling Leptin-Sensitive Neuronal Circuits Involved In Suppression Of Hyperactivity In Activity Based Anorexia

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Anorexia nervosa (AN) is a severe eating disorder characterized by excessive physical activity. Hyperactivity in AN negatively correlates with plasma leptin levels. Leptin suppresses hyperactivity in rodent anorexia models and has shown benefits in off-label AN treatment, suggesting its potential as a therapeutic target. This study aims to identify the leptin-sensitive neuronal circuits involved in hyperactivity suppression related to AN pathology. We focused on leptin's effect in the ventral tegmental area (VTA), substantia nigra (SN), and lateral hypothalamus (LH). To examine leptin's role, female Wistar rats underwent bilateral brain infusions of leptin while being exposed to activity-based anorexia (ABA) model, where food restriction and voluntary wheel running induce hyperactivity and severe weight loss. Primary outcomes were analyzed using repeated measures ANOVA. Leptin infusions in the LH and SN significantly suppressed hyperactivity (LH: n=22, $F(2,2)=5.235$, $p=0.010$; SN: n=32, $F(2,2)=7.690$, $p=0.001$), while no effect was observed for the VTA (n=36, $F(2,2)=1.143$, $p=0.325$). These findings contrast previous research highlighting the VTA's role, emphasizing the SN and LH as key players in leptin-mediated hyperactivity suppression. Next, chemogenetic manipulation of leptin receptor (LepR) expressing neurons was performed in female LepR-cre mice to determine their role in hyperactivity. Activation of SN LepR neurons significantly reduced hyperactivity ($T(13)=2.185$, $p=0.0478$), suggesting that leptin's effects extend beyond dopamine neurons and may involve GABAergic LepR neurons in the midbrain. This study provides new mechanistic insights into leptin's role in hyperactivity suppression in AN models and supports further investigation into its therapeutic potential.

P229 **Metabolic Processing In Taste Cells Contributes To The Hedonic Appeal Of Carbohydrates**

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Oral sensory and digestive processing of sugars directly affect downstream events like glucoregulation and satiation, but whether these events directly contribute to the hedonic appeal of sugar remains unknown. We showed that glucokinase (Gck) plays a role in the ability to detect free glucose and discriminate it from other sweeteners. Here, we investigated whether this novel glucose taste sensor is required to drive ingestion of more complex glucose-yielding carbohydrates, and high carbohydrate diets. We further assessed whether maltase glucoamylase (Mgam), which is expressed on taste cells, facilitates oral sugar sensing. Results showed that virogenetic knockdown of glucokinase in the major taste fields significantly attenuated licking responses for maltose in sweet sensitive and sweet-blind mice. Lingual Gck knockdown also impaired the immediate recognition of an ultra-processed diet enriched in maltodextrin and starch. To evaluate the hydrolysis of these complex carbohydrates we conducted molecular analyses on the taste papillae which revealed that reduced sweet receptor expression was associated with elevated levels of Mgam. We thus developed a virogenetic approach to selectively interfere with Mgam expression in the major taste fields. Lingual Mgam knockdown attenuated the immediate lick avidity for maltose and the ultra-processed diet. Lastly, we found that added carbohydrate in the diet, especially fructose, significantly upregulated Mgam expression in the taste papillae. 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.

P231 **Identification Of A Novel Subset Of Cold-Activated Hypothalamic Neurons That Stimulate Feeding**

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Rationale/premise: Growing evidence suggests that the hypothalamus plays an important role in linking thermoregulation to energy homeostasis. Our preliminary data indicate that neurons expressing tyrosine hydroxylase (TH) in the hypothalamus are activated in response to cold exposure. **Hypothesis:** Cold exposure activates a novel subset of hypothalamic TH neurons, and this population plays a role in the regulation of energy intake. **Procedures:** Adult male C57BL/6J mice were acutely exposed to either a cold (10 °C) or warm environment (30 °C) for 90 min. Animals were then sacrificed and hypothalamus collected and processed for immunohistochemical analysis of TH(+) and cFos, a marker for neural activation (n=7-8). To determine whether activation of periventricular hypothalamic nucleus $(PeVN)^{TH}$ neurons is sufficient to increase food intake, TH-Cre animals underwent microinjection of a Cre-inducible hM3Dq DREADD directed to the PeVN (n=7). **Results:** Cold exposure increased both the number and % of TH neurons expressing cFos selectively in the PeVN (22.5 ± 1.2% for cold vs. 5.0 ± 1.3% for warm, a ~4-fold increase; $p=0.0003$). In contrast, cFos expression was not increased by cold exposure in other hypothalamic TH-expressing subpopulations, including the paraventricular nucleus (PVN) (p=ns) and arcuate nucleus (ARC) (p=ns). Additionally, we found that relative to vehicle-treated controls, food intake was robustly increased following CNO-induced activation of $PeVN^{TH}$ neurons (0.94 ± 0.18g with CNO vs. 0.28 ± 0.09g with vehicle, a ~3-fold increase; $p<0.01$). **Conclusions/relevance:** These findings implicate a novel subset of cold-activated hypothalamic TH neurons in the regulation of food intake.

P233 **Peripheral And Central Metabolic Adaptations To Short- And Long-Term High-Energy Diet Exposure In Obesity Resistant And Prone Rats.**

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Prolonged high-energy diet (HED) intake leads to an obese phenotype and has been repeatedly associated with gliosis and a pro-inflammatory state leading to neuronal circuitry adjustments in the mediobasal hypothalamus (MBH). However, the precise timeline for the establishment of these changes remains poorly characterized. To investigate HED-induced adaptations, we used a polygenic rat model of obesity selectively bred to be resistant (DR) or prone (DIO) to HED-induced obesity. DR and DIO male rats were exposed to HED for different durations (1, 3, 7, 28 or 70 days). One group remained on chow for 10 weeks, and one was exposed to 4 weeks of HED prior being switched back to chow for 6 weeks. We monitored body weight and food intake, and assessed terminal metabolic parameters. To assess the effect of the phenotype in response to the diet, untargeted proteomics on plasma and MBH using LC-MS/MS was performed. Several metabolic markers (glucose, insulin and leptin levels, fat mass) worsened in DIO rats with increasing HED exposure duration, while DR rats showed a lower degree of impairment. DIO rats exposed to HED for 10 weeks exhibited less pronounced metabolic disruption than those exposed for 4 weeks, suggesting slow-establishing compensatory mechanisms. Despite reducing

caloric intake, switching back DIO rats to chow failed to restore metabolic parameters or limit subsequent weight gain compared to DIO rats kept on HED for 10 weeks. Preliminary plasma proteomics data reveal extensive differences in pathways affected in metabolic disorders between chow diet-fed DR and DIO rats. 3d of HED was sufficient to reverse the expression of the same pathways in DIO rats. After 10 weeks on HED, 3 times less differentially expressed proteins were found between the two phenotypes.

P235 **Targeting Nutrient-Induced Satiating Vagal Afferent Neurons Via Trap2 Mice.**

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The gut-brain neuronal axis is critical for control of food intake, as intestinal nutrients activate vagal afferent neurons to control meal size via release of gut peptides from enteroendocrine cells. However, the specific population of vagal neurons signaling pathways which mediate this response following nutrient ingestion is still not fully understood. We utilized TRAP2 ($Fos^{2A\text{-}iCreER}$) mice, coupled with a bilateral nodose injection of an excitatory DREADD (pAAV-hSyn-DIO-hM4D(Gq)-mCherry),and one week later were implanted with a small intestinal catheter. Following recovery, mice were overnight fasted and given an i.p. injection of 4-hydroxytamoxifen (4-OHT) immediately prior to small intestinal infusion of either saline ($Saline^{TRAP}$) or intralipid ($Lipid^{TRAP}$), resulting in Gq DREADD expression selectively in the vagal afferents neurons activated by infusion. For CCK experiments, CCK (CCK^{TRAP}) or PBS (PBS^{TRAP}) i.p. injection was given 30 min following 4-OHT administration, selectively targeting the DREADD to CCK-activated vagal afferent neurons. Utilizing these mice, we demonstrated that injection of DREADD agonist clozapine N-oxide (CNO) following a 12hr fast significantly decreased food intake in $Lipid^{TRAP}$ compared to $Saline^{TRAP}$ mice. Furthermore, CCK^{TRAP} mice exhibited a similar reduction in food intake in response to CNO, compared to PBS^{TRAP} animals. These data demonstrate the ability to selectively target nutrient-induced satiating vagal neurons *in vivo* and reveal that excitation of lipid-activated or CCK-activated vagal afferent neurons is sufficient to decrease food intake. Future studies will be aimed at better understanding these specific neuronal populations.

P237 **A Novel Immunotherapy Targeting Corticotrophin-Releasing Hormone Improves Weight Loss Quality In Obese Mice Treated With Semaglutide.**

Karen A. Scott[1,2], Jessica M. Sa[1,2], Todd E. Golde[3,4,5], Annette D. de Kloet[1,2], Eric G. Krause[1,2]

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Glucagon-like peptide 1 receptor (GLP-1R) agonists are highly effective for the treatment of obesity, but side effects like loss of lean mass can limit weight loss quality. Moreover, cessation of treatment results in rapid weight regain. GLP-1Rs are potent activators of the hypothalamic-pituitary-adrenal (HPA) axis, which may contribute to these effects. Here we assess whether CTRND05, an antibody targeting corticotrophin-releasing factor (CRF), can improve weight loss quality in obese mice given GLP-1R agonists and attenuate weight gain after treatment ends. Obese mice maintained on high fat diet were assigned to i.p. CTRND05 (25 mg/kg initial, 12.5 mg/kg weekly) or saline (SAL) administration based on initial body weight and composition. Following 1 wk of CTRND05 or SAL, all mice received daily injections of semaglutide (SEMA, 40 ug/kg, s.c.) for 3 wk. Following 1 wk of CTRND05, mice consumed less food than SAL mice, which was coupled with lower energy expenditure and oxygen consumption that lasted the duration of the study. Both groups ate less and lost a significant amount of weight following 1 wk of SEMA treatment, with CTRND05 eating significantly less than SAL mice. Both groups lost fat mass, but CTRND05 mice maintained more lean mass than SAL mice. At the end of SEMA treatment, CTRND05 mice weighed less than SAL and had better quality weight loss. 1 wk following SEMA cessation, SAL mice gained significantly more body weight, as both fat and lean mass, than CTRND05 mice. CTRND05 mice regained body weight, primarily as lean mass and continued to eat less and expend less energy than SAL mice. These data suggest that targeting the HPA axis may promote better quality weight loss and blunt hyperphagia and fat gain that occurs following cessation of GLP-1R treatment.

P239 **Methods To Measure Concentration Of Artificial Sweeteners In Plasma**

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Artificial sweeteners are widely used in the U.S., yet their metabolic effects remain unclear. While studies have examined their impact on metabolic markers like insulin, few have directly measured their plasma concentrations post-consumption. This study develops a method for quantifying artificial sweeteners in blood following ingestion of a beverage similar to those already on the market. We hypothesize that artificial sweetener concentrations in plasma will follow a time-concentration curve, increasing over time after ingestion, and may exhibit metabolic interactions with nutritive sweeteners. Thirty participants will consume one of three beverages: (1) sucralose/acesulfame potassium (AceK), (2) sucrose, or (3) a combination of sucralose, AceK, and sucrose. Blood samples will be collected at baseline and at 5, 10, 30, 60, 90, and 120 minutes post-consumption. Plasma concentrations will be analyzed using gas chromatography-mass spectrometry (GC-MS) with a validated extraction and derivatization protocol. Multiple reaction monitoring mode will enhance detection sensitivity and specificity. A within- and between-subjects study design will be used, with data analyzed via linear regression and mixed-effects models. Preliminary data show sucralose concentrations ranging from 3.91 ng/mL at baseline to 143 ng/mL at 60 minutes, with successful conversion to its 5-TMS analog for GC-MS quantification. These values align with prior studies, though fluctuations suggest metabolic or sampling variability. Establishing a reliable method for measuring artificial sweeteners in plasma will facilitate future research on artificial sweeteners' metabolic effects and interactions with nutritive sweeteners, with further refinement needed to address unexpected concentration variations.

P241 **Preliminary Reliability Of A Food Images Questionnaire For Children Aged 6-11 Years**

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Rationale: Food images are commonly used as a virtual substitute for real food when collecting dietary intake information, as children may struggle to recall accurately and consistently. Developing a culturally adapted food image questionnaire for children presents challenges regarding food identification, representability, and variety across different eating habits. **Hypothesis:** Culturally valid food images tailored to Israeli children aged 6–11 will demonstrate high reliability and validity. **Species:** Human **Participants:** Fifteen pediatric dietitians evaluated the content validity. A pilot study conducted through online interviews included 10 healthy children-parent dyads (children aged 6-11). **Methods:** A comprehensive food list was compiled based on the Ministry of Health's food groups, ensuring representation of the entire Israeli diet across all groups. Food images were photographed under standard conditions. Content validity and item shortlisting were conducted through expert evaluation. Assessment by 15 dietitians led to removing 50% of items based on Lawshe's content validity ratio (CVR <0.5). Face validity was tested with 10 parent-child dyads through video interviews. **Main Outcome Measures:** The content validity of food images was assessed using CVR. **Statistical Analysis:** Lawshe CVR was used for assessment. **Preliminary Results:** The final 50-item questionnaire was tested. Duplicate items (e.g., sliced cucumber and cucumber salad) were removed. Eighty percent of images were correctly identified. Interviews lasted 40 minutes, which led to participant fatigue. **Conclusions and Significance:** The food image database demonstrates validity and cultural relevance. Further testing in a larger sample is needed to confirm its reliability and validity.

10:00 - 11:30 AM	L1
Symposium 2: GLP-1R agonists: what can we learn from these drugs? (Sponsored by Novo Nordisk)	

Chair(s): Joerg Hoeck

10:00 **Effects Of Semaglutide On Wheel Running And Associated Dopamine Dynamics In Mice**

E.P. Foscue[1], R. TRINKO[1], E. KONG[1], J. LARA JIMENEZ[1], K. STANKEWICH[1], S.L. THOMPSON[1], A. CORSTENS[1], M.J. SERLIE[4], J.R. TAYLOR[1,2,3], R.J. DILEONE[1,2,3]

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Glucagon-like peptide-1 (GLP-1) receptor agonists are effective anti-obesity agents that act via reduction in food intake. There is also evidence for drug and alcohol intake with less known about non-ingestive behavioral outcomes. We examined the effects of the long-acting GLP-1 receptor agonist semaglutide on voluntary wheel running and motivation to run in mice. In both lean and diet-induced obese (DIO) mice, semaglutide suppressed voluntary running behavior, independent of weight loss or caloric restriction. To directly assess motivation to run, we employed a progressive ratio operant task in which mice nose-poked to gain wheel access; semaglutide significantly reduced operant responding in both dietary conditions. No differences in semaglutide effects were observed between lean and DIO mice, and males and females both showed similar responses. Running bout analysis demonstrated that semaglutide causes a reduction in running bout length with no changes in bout number. Ongoing fiber photometry studies indicate that semaglutide modifies dopamine dynamics during both the beginning and end of running bouts. These results expand our understanding of the broader behavioral effects of GLP-1 receptor agonists and identify potential mechanisms by which semaglutide modifies reward-related behaviors.

10:30 **Targeting Stress Axes To Enhance The Therapeutic Efficacy Of Glp-1R Agonists.**

Jessica M. Sa[1,2], Karen A. Scott[1,2], Todd E. Golde[3], Eric G. Krause[1,2], Annette D. de Kloet[1,2]

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Obesity is highly prevalent worldwide. While glucagon-like peptide 1 receptor (GLP-1R) agonists reduce body weight in the short term, side effects (e.g., lean mass loss) and a tendency for individuals to regain fat mass after withdrawal limit their long-term benefit. We hypothesize that hypothalamic-pituitary-adrenal (HPA) axis dysregulation contributes to these limitations. GLP-1R agonists activate the HPA axis and corresponding increases in glucocorticoids (CORT) alter food intake and body composition. We use a novel anti-corticotrophin-releasing hormone (CRH) immunotherapy (CTRND05) to test whether dampening HPA axis activity enhances and sustains quality weight loss during and following semaglutide. Male and female C57BL/6J mice were rendered obese on high fat diet, housed in an indirect calorimetry system and assigned to four groups: 1) saline, 2) semaglutide (40ug/kg/d sc), 3) CTRND05 (25 mg/kg ip, followed by weekly 12.5 mg/kg), or 4) combination semaglutide/CTRND05. Metabolic parameters, plasma CORT and glucose tolerance were assessed prior to, during and following 3 weeks of semaglutide.As expected, CTRND05 reduced plasma CORT throughout the study.Semaglutide, alone and in combination with CTRND05, reduced body and fat mass. Furthermore, semaglutide resulted in considerable loss of lean mass, an effect abated by CTRND05. After discontinuing semaglutide, mice exhibited pronounced hyperphagia and regained adiposity. Both hyperphagia and adipose mass regain were mitigated by combined treatment with CTRND05. Collectively, these results indicate that the negative side effects of GLP-1R agonists can be mitigated by suppressing HPA axis activity, and further suggest that quality weight loss can be enhanced and sustained by interventions that lower circulating CORT.

11:00 ***Can Weight Loss Drugs Reduce Alcohol Consumption?***

Mette Kruse Klausen
Psychiatric Centre Copenhagen, Mental Health Services in the Capitol Region of Denmark, Copenhagen University Hospital Frederiksberg, Frederiksberg, Denmark

Alcohol use disorder (AUD) is a chronic relapsing brain disorder characterised by loss of control of alcohol intake, compulsive alcohol behaviour leading to relapse, and a negative affective state when not consuming alcohol. Globally, AUD is a tremendous burden, with an estimated 280 million people suffering from this disorder, and the treatment gap is wide compared to other mental health disorders. In this perspective, AUD is a severe condition with enormous consequences for the individual, relatives, and society, and is regarded as the most harmful addictive drug when taking harm to both the user and others into consideration. According to clinical guidelines, a combination of psychological intervention and pharmacological treatment is recommended in patients with moderate to severe AUD. However, only three drugs are approved by the U.S. Food and Drug Administration. In the search for novel treatment strategies for AUD, glucagon-like peptide-1 (GLP-1) receptor agonists approved for treating type 2 diabetes and obesity have caught much attention. GLP-1 is a naturally occurring peptide produced in the small intestines and in the brain, regulating glucose homeostasis, feeding, and body weight. Importantly, recent research demonstrates that GLP-1 also acts within brain regions involved in reward and addiction. This session will introduce the present data from preclinical studies, register-based cohort studies, brain imaging, and clinical data, all supporting the role of GLP-1 receptor agonists as a novel treatment of alcohol use disorder.

10:15 - 11:30 AM	L2
Oral Session 4: Know thyself; interoception and ingestion	

Chair(s): Amanda Page

10:15 **Vagal Sensory Neurons Selectively Encode Intestinal Protein**

Alan de Araujo[1,2], Mingxin Yang[1,2], Avnika Bali[1,2], James McCutcheon[4], Christopher Morrison[3], Guillaume de Lartigue[1,2]
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Dietary protein is essential for survival and generally palatable, though less reinforcing than fats or sugars. When protein intake is restricted, animals rapidly increase consumption of protein-rich foods, suggesting that animals can detect protein deficiency and adapt their intake accordingly. However, the neural circuits that sense ingested protein and guide this adaptive behavior remain poorly defined. *We hypothesized that a specific population of vagal sensory neurons detects dietary protein and transmits this signal to the brain to influence protein appetite*. **Results:** To manipulate protein status, mice were maintained on a low-protein diet (5% casein) to induce a protein-depleted state, or a control diet (20% casein) to maintain protein repletion. *In vivo* calcium imaging of the nodose ganglia revealed that intestinal casein infusion activates a subset of vagal sensory neurons, with enhanced responses in protein-depleted mice (n=382-512 neurons, $p<0.05$). Consistently, within-animal FosTRAP mapping revealed greater NTS activation in response to casein infusion during protein depletion compared to repletion (n=5). In two-bottle behavioral tests, control mice increased casein intake when protein-depleted ($p<0.05$). Mice lacking protein-sensing vagal neurons exhibited elevated casein consumption regardless of diet, suggesting impaired detection of protein status. Upon switching from a depleted to a replete diet, control mice reduced casein intake ($p<0.01$), with females adapting to changes in protein status quicker than males (7 vs 14 days). In contrast, ablated mice failed to adapt at all time points ($p<0.05$). **Conclusion:** These findings identify a vagal gut-brain pathway that detects dietary protein and influences protein appetite through post-ingestive feedback.

10:30 **A Dedicated Gut-Brain Pathway For Hypothalamic Fructose Sensing**

Aaron D Mcknight[1,2], Fang Y Hsu[2], Alexandra G Vargas[2], Alan Araujo[2], Guillaume Lartigue[1,2], Amber L Alhadeff[1,2]
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Activity in hypothalamic agouti-related protein (AgRP)-expressing neurons drives food intake and is inhibited by the post-ingestive detection of calories. Given that our modern diets contain increasing levels of added sugars, we examined how glucose and fructose impact activity in AgRP neurons. We monitored AgRP neuron activity using *in vivo* fiber photometry, and surprisingly found that equicaloric quantities of fructose (8% and 16% w/v, 1 ml intestinal infusion) were much less effective than glucose at inhibiting AgRP neuron activity (n=10, two-way ANVOA $p<0.05$). The time to maximally inhibit AgRP neuron activity was longer after fructose compared to glucose infusion, suggesting that fructose may modulate AgRP neurons in a paracrine fashion (n=10, two-way ANOVA $p<0.05$). Therefore, we measured levels of satiation hormones after a gastric infusion of either sugar and found that fructose evokes 10-fold higher levels of plasma peptide YY (PYY) than glucose (n=11-13/group, one-way ANOVA $p<0.0001$). Pretreatment with a systemic (paired t-test $p<0.05$), but not centrally-infused (n=6, paired t-test p=ns), Y2 receptor antagonist, or elimination of vagal signaling by subdiaphragmatic vagotomy (n=4-6/group, unpaired t-test $p<0.05$) abolished fructose, but not glucose, -induced inhibition of AgRP neuron activity. Finally, *in vivo* imaging of vagal afferents revealed distinct subpopulations that are activated (defined as mean z-score during stimulation>2.5 from baseline median) to either fructose (n=45) or glucose (n=56), with few (n=13) neurons responding to both. Therefore, our data reveal that fructose engages a distinct gut-to-hypothalamic pathway and is less effective than glucose at inhibiting AgRP neurons, a finding that may impact feeding behavior and obesity development.

10:45 **Sex-Specific Differences In Postprandial Satiety Signaling After A Sugar-Reduced Sucrose Solution While Maintaining Sweetness Level**

Marlies Gaider[1,3,6], Isabella Kimmeswenger[2,3], Jana Medek[1], Moritz Gaupp[1], Jakob P. Ley[4], Gerhard E. Krammer[4], Veronika Somoza[5], Barbara Lieder[1,2,6]
[1]Christian Doppler Laboratory for Taste Research, Faculty of Chemistry, University of Vienna, Vienna, Austria, [2]Institute of Physiological Chemistry, Faculty of Chemistry, University of Vienna, Vienna, Austria, [3]Vienna Doctoral School of Chemistry (DoSChem), Vienna, Austria, [4]Symrise AG, Holzminden, Germany, [5]Leibniz Institute for Food Systems Biology at the Technical University of Munich, Freising, Germany, [6]Institute of Clinical Nutrition, University of Hohenheim, Stuttgart, Germany

Sweetness perception is discussed to interfere with postprandial glucose and insulin regulation. This study examined whether maintaining perceived sweetness while reducing the sucrose content of a test solution affects incretin hormone secretion and blood sugar control with consequences for energy intake and whether sex-specific differences exist. We hypothesized that the carbohydrate content plays a stronger role than the perceived sweetness for inducing postprandial satiety signaling. In a single-blinded, randomized crossover study, 39 healthy participants (21 female, 18 male), consumed a 10 % sucrose solution, an equi-sweet tasting 7 % sucrose solution with 50 mg/L hesperetin and a less sweet tasting 7 % sucrose solution. Blood samples were collected at baseline and 15, 30, 60, 90 and 120 minutes postprandial and energy intake was assessed using a standardized ad liibitum breakfast 2 hours postintervention. Female participants exhibited lower glucose peaks after consuming the sucrose-reduced solutions. However, males reached similar glucose peaks independent of the test solution, explained by higher insulin concentrations following the 10 % sucrose solution. GLP-1 concentrations were higher in females after consuming the 10 % sucrose and hesperetin-spiked solutions but remained unaffected in males. In contrast, GIP levels were higher in males after the two equi-sweet solutions compared to the 7% sucrose treatment. Energy intake did not differ between the different treatments. Our findings demonstrate sex-specific differences in postprandial glucose regulation and incretin hormone responses. However, maintaining sweetness level while reducing sucrose content did not adversely affect satiety signaling or energy intake in both female and male participants.

11:00 **Temporal Control Of Snacking And Body Weight By Ghsr-Expressing Suprachiasmatic Nucleus Neurons**

Omprakash Singh[1,2], Sepideh Sheybani-Deloui[1], Soumya Kulkarni[1], Moyu Lyu[1], Bingbing Li[1], Salil Varshney[1], Kripa Shankar[1], Deepali Gupta[1], Luis Leon Mercado[1], Avi W. Burstein[1], Corine P. Richard[1], Connor Lawrence[1], Sherri Osborne-Lawrence[1], Jeffrey M. Zigman[1,2,3]
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United States, [2]Peter O'Donnell Jr. Brain Institute, UT Southwestern Medical Center, Dallas, TX, United States, [3]Division of Endocrinology & Metabolism, Department of Internal Medicine, UT Southwestern Medical Center,, Dallas, TX, United States, [4]Department of Psychiatry, UT Southwestern Medical Center,, Dallas, TX, United States

Food consumption impacts body weight differently depending on time-of-day. Exemplifying this concept, providing mice or people food during their usual circadian rest phase (light cycle for mice; night-time for people) leads to greater body weight gain than providing it during the active phase. This suggests the existence of specific neurocircuitry that impacts eating and body weight in a manner dependent on circadian phase/time-of-day. One such neurocircuit may reside in the suprachiasmatic nucleus (SCN), the body's central circadian pacemaker. Here, we tested the hypothesis that SCN neurons responsive to the orexigenic hormone ghrelin temporally regulate eating and body weight in mice. Chemogenetic stimulation of GHSR (ghrelin receptor)-expressing SCN neurons during the mid-circadian rest phase (10AM-2PM) - which is a period of low ghrelin resistance - increased food intake by 144% ($p<0.05$; n=4; paired Student's t-test). Repeated chemogenetic inhibition of these neurons during this same time-of-day reduced (by 35%) the corresponding, typically low level of food intake reminiscent of snacking; it also reduced body weight (by 7%) ($p<0.05$; n=6-9). These effects were not observed at other times-of-day. Chemogenetic stimulation of GHSR-expressing arcuate hypothalamic neurons also increased food intake, although independently of time-of-day ($p<0.05$; n=3-4). GHSR-expressing SCN neurons represented subpopulations of six distinct SCN neuronal clusters, were predominantly GABAergic, and exhibited light-sensitive, time-of-day-dependent transcriptomic profiles. Thus, our study identifies GHSR-expressing SCN neurons as a neuronal population that regulates snacking during the mid-circadian rest phase and accounts for a small but not insignificant proportion of a mouse's body weight.

11:15 **From Stomach To Striatum: Ghrelin Infusions Increase Work For Rewards**

Corinna Schulz[1,2], Franziska Peglow[1], Christian La Fougere[3], Benjamin Bender[4], Johannes Klaus[1], Martin Walter[5,6,7], Matthias Reimold[3], Nils B Kroemer[1,2,8]

[1]Department of Psychiatry and Psychotherapy, Tuebingen Center for Mental Health, University of Tuebingen, Tuebingen, Germany, [2]Section of Medical Psychology, Department of Psychiatry and Psychotherapy, Faculty of Medicine, University of Bonn, Bonn, Germany, [3]Nuclear Medicine and Clinical Molecular Imaging, Department of Radiology, University of Tuebingen, Tuebingen, Germany, [4]Diagnostic and Interventional Neuroradiology, Department of Radiology, University of Tuebingen, Tuebingen, Germany, [5]Department of Psychiatry & Psychotherapy, University Hospital Jena, Jena, Germany, [6]Department of Behavioral Neurology, Leibniz Institute for Neurobiology, Magdeburg, Germany, [7]German Center for Mental Health (DZPG), partner site Jena-Magdeburg-Halle, Germany, [8]German Center for Mental Health (DZPG), partner site Tuebingen, Germany

Preclinical evidence demonstrates that the stomach-derived hormone ghrelin increases work for food via the dopaminergic system. However, translational research in humans is scarce, and it is not known if surges of ghrelin acutely boost motivation via increases in dopamine. To close this gap, we investigated the effects of acyl ghrelin infusions (vs. saline) on instrumental work for rewards, functional connectivity (FC), and dopamine transmission using a double-blind, randomized crossover study with ^{11}C-raclopride PET-fMRI in 26 healthy human volunteers. First, ghrelin increased subjective ratings of hunger ($b = 15.87$, $p = .007$) and instrumental effort for food ($b = 2.12$, $p = .045$) as well as small rewards ($b = 2.80$, $p = .043$), indicative of a shift in motivation. Second, we tested if ghrelin enhanced hypothalamic or nucleus accumbens (NAcc) seed-based FC. Ghrelin increased FC between the hypothalamus and striatal regions (NAcc: $t_{max} = 3.36$, $p_{SVC} = .016$; caudate: $t_{max} = 3.79$, $p_{SVC} = .019$), as well as within the striatum (NAcc-putamen: $t_{max} = 4.78$, $p_{SVC} = .001$), demonstrating an enhanced coupling between homeostatic and motivational circuits. Third, we investigated if ghrelin decreased striatal dopamine binding potential (BP_{ND}) which would reflect increases in endogenous dopamine tone. Although ghrelin increased BOLD responses in the midbrain during effort ($t_{max} = 4.10$, $p_{SVC} = .002$), it did not alter BP_{ND} in the striatum ($N = 20$, sample will be completed), suggesting that ghrelin does not durably increase striatal dopamine tone. We conclude that ghrelin's effects on motivation show an increase in the value of work for rewards, specifically food, highlighting the potential of targeting gut-brain interactions to improve motivational symptoms, such as loss of appetite.

11:30 - 1:00 PM	On Own
Lunch	

11:30 - 11:45 AM	L1
Innovation through Collaboration - Novo Nordisk Partnership Models	

Chair(s): Joerg Hoeck

11:30 **Innovation Through Collaboration - Novo Nordisk Partnership Models**
JOERG HOECK
Novo Nordisk A/S

11:45 - 12:55 PM	L2
Professional Development Event, organized by the New Investigator Advisory Committee	

Join us for a panel presentation on the principles of open science and how they are applied at the frontiers of ingestive research in both clinical and preclinical models.

This will be followed by an open discussion on the current and projected landscape of open science.

Lunch provided afterward for 65 registrants.

We ask new investigators to sign up for this event using the following link: https://linkyme.com/?NIACPD.

11:45 **Open Science And Open Source Tools Seminar**

1:00 - 1:55 PM	L1
MARS Lecture 2 - John Glendinning, Barnard College	

Chair(s): Lindsey Schier

1:00 **Functional Properties Of The Cephalic-Phase Insulin Response In Mice**
John Glendinning
Barnard College, Columbia University, New York, NY, United States

Mammals have evolved a variety of feed-forward mechanisms that minimize disturbances to their internal milieu. For example, to limit the rise in blood glucose during and after meals, mammals elicit rapid increases in celiac artery blood flow, celiac artery vascular conductance, and insulin secretion. Because these responses are triggered by stimulation of sensory systems in the head (e.g., vision, olfaction and taste), they are called cephalic-phase responses. Over the past decade, my colleagues and I have examined the functional properties of the cephalic-phase insulin response (or CPIR) in mice. I will address five facets of this work. (1) What is the physiological significance of CPIR? We determined that (as in other mammals) CPIR markedly enhanced glucose tolerance. We also observed large individual differences in CPIR magnitude, and that those mice with larger CPIR magnitudes exhibited better glucose tolerance. (2) Does CPIR magnitude vary with diet? We discovered that CPIR magnitude and glucose tolerance increased with carbohydrate content of the diet. (3) What stimuli elicit CPIR? In naïve mice, we found that CPIR could be elicited by oral stimulation with glucose or glucose-containing carbohydrates, but not with fructose, sweeteners or novel types of mouse chow. (4) To what extent can CPIRs be conditioned? We found that mice could condition CPIRs to mouse chows and to flavors associated with the post-oral actions of concentrated glucose. (5) When mice condition a CPIR to one food, does it generalize to other foods? We discovered that a conditioned CPIR to one type of chow did not generalize to another type of chow with the same macronutrient composition. The latter finding revealed a high degree of diet specificity in the CPIR conditioning process.

2:00 - 4:00 PM	L1
New Investigator Travel Award (NITA) Symposium	

Chair(s): Kathleen Keller

2:00 **Relationships Between Increasing Pre-Load Meal Size, Post-Prandial Plasma Acyl Ghrelin, Appetite, And Food Intake In Adults Without Obesity - Is Ghrelin A Human Satiety Signal? (George H. Collier New Investigator Travel Awardee)**

Tasya Parastika[1], Jiaxyn Liu[1], Raghav Bhargava[1], Wai In Ng[1], Jialin Guo[1], Marcela Rodriguez Flores[1], Xinyi Zhang[1], Mimoza Emini[1], Wanqian Li[1], Sandra Luur[1], Zoe Barley[1], Jeff Brunstrom[2], Anthony P Goldstone[1]
[1]PsychoNeuroEndocrinology Research Group, Division of Psychiatry, Department of Brain Sciences, Imperial College London, London, United Kingdom, [2]School of Psychological Science, University of Bristol, Bristol, United Kingdom

Background: Stomach-derived acyl ghrelin (AG) stimulates human appetite/food intake from studies of supra-physiological AG administration, but correlational studies of endogenous plasma AG with eating behaviour are contradictory. Plasma total

ghrelin falls with increasing pre-load meal size in adults without obesity, but it is unclear if this contributes to post-prandial attenuation of eating behaviour. **Methods:** In a randomised, single-blinded study, n=17 adults without obesity (53% male, age 21-55 years) attended 4 visits after an overnight fast, consuming 750mL liquid preloads 0, 600, 900, 1200 kcal. At 0, 0.5, 1, 2, 3h plasma AG was assayed, and appetite and food craving ratings completed (n=17, 65 visits). At 2h a virtual portion size creation task measured desired food intake (n=15, 57 visits), and at 3h an *ad libitum* meal measured actual food intake (n=10, 39 visits), with data excluded for those participants with intake <20% estimated REE at 0 kcal visit. **Results:** Pre-load meal size correlated negatively with post-prandial changes ($iAUC_{0\text{-}2/3h}$) in appetite, craving, desired and actual caloric intake (r=-0.55 to -0.38, P=0.010 to <0.001). Plasma AG $iAUC_{0\text{-}3h}$negatively correlated with pre-load size (r=-0.53, P<0.001) and positively correlated with post-prandial changes in appetite/craving (r=0.33-0.34, P<0.005), desired (r=0.33, P<0.005), and actual (r=0.26, P<0.05) food intake. **Conclusion:** The post-prandial fall in plasma AG may contribute to the greater attenuation of eating behaviour with increasing preload meal size in adults without obesity, supporting a role for changes in plasma AG as a human satiety signal. Ongoing assay of plasma hormone LEAP2, an inverse agonist at ghrelin receptor (GHSR), is examining its additional potential as a satiety hormone by impacting GHSR signalling.

P2
2:15

A Cerebellar Memory Of A Meal (New Investigator Travel Awardee)

A-Hyun Jung[1], Aloysius Y.T. Low[1], J. Nicholas Betley[1,2]

[1]Department of Biology, University of Pennsylvania, Philadelphia, PA, United States, [2]Department of Neuroscience, University of Pennsylvania, Philadelphia, PA, United States

Cerebellar output neurons have recently been shown to regulate food intake. To further explore the function and characteristics of cerebellar output neurons activated during the course of the meal, we used Fos-TRAP technology to permanently label neurons in the cerebellum activated by a meal. We used $Fos^{2A\text{-}iCreER}$ mice to express chemogenetic actuators or calcium indicators in the lateral deep cerebellar nuclei (latDCN) neurons activated during high fat diet refeeding after 24hr fasting. Chemogenetic activation, but not inhibition, of the latDCN meal engram reduced the food intake in 1hr and 3hr food intake measures. Importantly, activating the latDNC meal engram did not affect energy expenditure in metabolic chamber or motor functioning in motor activity assessments. Using fiber photometry calcium imaging, we found that neural activity in the latDNC meal engram is suppressed while the mice eat food pellets. Notably, intraperitoneal injection of post-prandial hormone insulin and CCK, but not the hunger hormone ghrelin, activated the latDCN meal engram. Glucose and 2-DG injection, which both increase plasma glucose level, raised the activity of latDCN meal engram neurons. Fluorescence in situ hybridization showed that the latDCN meal engram neurons highly express vGLUT2 and SPP1. Together, these results characterize a population of latDCN neurons that comprise a memory of a meal.

P3
2:30

Resilience Amidst Adversity: How Adverse Childhood Experiences And Protective Factors Influence Body Weight Status In Latinx/Hispanic Youth (New Investigator Travel Awardee)

Victoria Goldman[1], Sevan Esaian[1], Jonatan Ottino Gonzalez[1], Miguel A. Rivas Fernandez[1], Nicole R. Karcher[2], Jeffrey I. Gold[1], Alaina P. Vidmar[1], Shana Adise[1]

[1]Children's Hospital Los Angeles, Los Angeles, CA, United States, [2]Washington University School of Medicine, St. Louis, MO, United States

Adverse childhood experiences (ACEs) may contribute to rising youth obesity rates through stress-induced weight gain via hormonal dysregulation and altered food intake. Few studies have explored this association in youth including what protective factors (PF) may mitigate it. Even less is known about these associations in Latinx/Hispanic (LH) communities, despite higher ACEs and obesity rates. Using the Adolescent Brain Cognitive Development Study (n=5,435; age 11-12; 51% male; 21% LH), we explored associations between ACEs, PF, and BMI. We hypothesized that higher ACEs would be associated with greater BMI but weakened by PF (youth-reported self-coping, friend or caregiver support). We anticipated stronger findings in LH youth. ACEs comprised 12 categories (e.g., sexual abuse, bullying) from caregiver or youth answers, summed to a total score. Linear mixed-effects examined ACE*Ethnicity (LH vs. non-LH)*PF on BMI, controlling for age, sex, puberty, socioeconomic status and study site. We found that higher ACEs were associated with greater BMI (β_{LH}=0.56; $\beta_{non\text{-}LH}$=0.38, p<0.001). LH youth had greater BMI (22.1$\pm$5kg/m^2) and ACEs (2.1$\pm$1.7) than non-LH youth (BMI=20.3$\pm$4.6kg/m^2; ACEs=1.7$\pm$1.7; p<0.001). In LH youth only, self-coping (β=-0.65) and caregiver-support (β=-0.33) moderated the ACE-BMI relationship (p's<0.05). Our findings suggest ACEs increase youth obesity risk, while two PF weaken the ACE-BMI relationship in LH youth. This highlights the importance of promoting culturally informed, resiliency-focused skills like self-coping and positive adult relationships, particularly among LH-youth experiencing ACEs. Early ACE screening to identify at-risk youth, coupled with PF promotion and trauma-informed weight interventions, may help improve pediatric weight trajectories.

P4
2:45

Improved Food Approach Following Weight Restoration With Meal-Based Behavioral Treatment In Inpatients With Anorexia Nervosa. (New Investigator Travel Awardee)

Sarah H Guo[1], Joseph McGuire[1], Jeffrey M Brunstrom[2], Timothy H Moran[1], Angela Guarda[1], Kimberly R Smith[1]

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

Individuals with anorexia nervosa (AN) often experience marked anxiety when consuming high energy-dense (HED) foods. This anxiety leads to the avoidance of HED foods, which interferes with recovery. Weight restoration is the strongest predictor of recovery and remission in AN. Despite treatment advances, empirical evidence of changes in food preference and consumption during recovery remains limited. The Johns Hopkins Eating Disorders Inpatient Program employs a meal-based behavioral protocol to increase consumed food variety and achieve rapid weight restoration. We recruited women with AN (N=21) admitted to this program to determine the effect of a meal-based approach on food liking and wanting, anxiety-to-eat, perceived maximum tolerable portion size and food healthiness. Following an overnight fast, participants completed a computer task featuring images of 10 HED and 10 low energy-dense (LED) foods across five portion sizes (standard * 0.25, 0.5, 1, 2, 4) on two occasions: shortly after hospital admission (T1) and again upon reaching weight restoration (T2). At T2, participants reported increases in the consumption of and maximum tolerable portion size of HED foods. This change was accompanied by increased wanting for and decreased anxiety-to-eat HED foods. For LED foods, anxiety-to-eat decreased while wanting remained unchanged. Food liking and perceived healthiness of HED and LED foods did not change with

weight restoration. These findings suggest that meal-based nutritional and behavioral interventions targeting increased variety of HED and LED food intake may improve food approach (reduce anxiety-to-eat, increase wanting) while maintaining food stable perception (liking, healthiness) in individuals with AN hospitalized for acute weight restoration.

P5
3:00

From Metabolism To Memory: Exploring Amylin'S Role In The HippocampusÂ (New Investigator Travel Awardee)

Giulia Mazzini[1], Irmak Gezginer[2,3], Gaia Serra[1], Diana Kindler[2], Christelle Le Foll[1], Daniel Razansky[2, 3], Thomas A. Lutz[1]

[1]Institute of Veterinary Physiology, Vetsuisse Faculty, University of Zurich, Zurich, Switzerland, [2]Institute for Biomedical Engineering and Institute of Pharmacology and Toxicology, Faculty of Medicine, University of Zurich, Zurich, Switzerland, [3]Institute for Biomedical Engineering, Department of Information Technology and Electrical Engineering, ETH , Zurich, Switzerland

Amylin, a hormone co-secreted with insulin by pancreatic β-cells in response to nutrient intake, acts as a satiation signal. Amylinomimetics are approved treatments for diabetes and in the future most likely for obesity management thanks to their effects on appetite and glucose metabolism. Although amylin's effects on eating behavior are well-documented, its broader physiological functions still need to be uncovered. Here, we investigated amylin's role in hippocampal function and memory processing. Using resting-state fMRI, we examined how amylin (500 μg/kg) and a long-acting amylin receptor agonist salmon calcitonin (sCT; 10 μg/kg) affect hippocampal connectivity in wild-type (WT) mice compared to knock-out (KO) mice lacking amylin receptor fundamental components (RAMP1/3). Both compounds induced significant changes in hippocampal connectivity patterns in WT mice but not in KO mice, highlighting the critical role of intact amylin receptor signaling in mediating these responses. c-Fos expression in the hippocampus was higher in amylin-injected and sCT-injected mice than in vehicle-injected mice, suggesting increased neuronal activation in this area. Through novel object and novel location recognition behavioral studies, we showed that amylin-treated WT mice significantly improved object recognition and spatial memory, while sCT treatment did not enhance memory performance. In a rat model both amylin- (50 μg/kg) and sCT-injected (5 μg/kg) rats demonstrated an improved ability to recognize objects and spatial locations compared to vehicle-injected rats. Our findings reveal amylin as a significant modulator of hippocampal function and memory processing, suggesting its potential therapeutic applications for both metabolic and cognitive disorders.

P6
3:15

Mapping Energy Metabolism Pathways In The Human BrainÂ (Elsevier Appetite New Investigator Travel Awardee)

Moohebat Pourmajidian[1], Justine Y. Hansen[1], Golia Shafiei[2], Bratislav Misic[1], Alain Dagher[1]

[1]McGill University, Montreal, QC, Canada, [2]McGill University, Montreal, QC, Canada, [3]University of Pennsylvania, Philadelphia, PA, United States, [4]McGill University, Montreal, QC, Canada, [5]McGill University, Montreal, QC, Canada

Energy metabolism consists of a set of biological pathways that produce ATP using nutrients such as glucose and oxygen. These pathways also provide biomolecules critical for cellular growth and repair, making them integral to our understanding of brain structure and function. Despite extensive studies on brain glucose uptake, the organization of downstream glucose metabolic pathways in the cortex remains largely unexplored. Here, we use whole-brain transcriptome data from 6 donors (1 female, 24-57 years) in the Allen Human Brain Atlas to study spatial cortical profiles of key energy pathways including glycolysis, pentose phosphate pathway, tricarboxylic acid cycle, oxidative phosphorylation and lactate metabolism. We create regional mean-expression maps of these pathways across the cortex using pathway-specific gene expression data. We show that energy pathways exhibit heterogenous cortical gene expression, with a dichotomy between primary ATP-producing pathways and the anabolic pentose phosphate pathway in the primary motor and sensory cortices, reflecting information processing hierarchy. These maps also exhibit unique relationships with the cellular and laminar organization of the cortex, pointing to higher energy demands of large pyramidal cells. Finally, we show that energy pathways exhibit unique developmental trajectories using a lifespan transcriptomics dataset of the human brain (42 donors, 19 female, 8 post conception weeks-40 years). The main ATP-producing pathways peak in childhood, tracking cortical volume, while the pentose phosphate pathway shows greater prenatal expression and declines in later life, mirroring brain tissue biosynthesis. Collectively, this study provides insight into the metabolic makeup of the human brain and its developmental demands.

P7
3:30

The Estrous Cycle Moderates The Food And Body Weight Suppressive Effects Of Glucagon-Like Peptide-1 Receptor Agonism (Randall R. Sakai New Investigator Travel Awardee)

Sarah V Applebey, Allison G Xiao, Matthew R Hayes
Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States

Among young adults, women largely drive demand for weight loss pharmacotherapies targeting the glucagon-like peptide-1 receptor (GLP-1R). Clinical trials for many GLP-1R analogs (GLP-1RAs) have revealed a curious sex difference: women lose a greater percentage of weight compared to men. Despite the popularity of GLP-1RAs, the mechanism(s) underlying women's enhanced weight loss is unclear. Recently, we identified evidence pointing to the estrous cycle as a mediator of this effect. In female rats, expression of *Glp1r* and the GLP-1 precursor gene, *Gcg*, increased during two estrous phases, proestrus and estrus (P/E), compared to males and compared to other estrous phases, metestrus and diestrus (M/D). These expression changes occurred in the nucleus tractus solitarius and area postrema within the brainstem's dorsal vagal complex (DVC), an intriguing finding given the necessity of DVC GLP-1Rs in the weight loss effects of GLP-1RAs. We hypothesized that greater endogenous GLP-1 or GLP-1R during P/E may potentiate effects of GLP-1RAs. To examine whether the estrous cycle impacts efficacy of GLP-1RAs, we administered acute liraglutide and chronic semaglutide during either P/E or during M/D in female rats on high fat diet. In both studies, injections during P/E enhanced the intake-suppressive effects of GLP-1RAs. Moreover, chronic semaglutide administration during only P/E led to pronounced body weight loss compared to M/D administration. We also identified additional nuclei throughout the neuraxis that showed greater in *Glp1r* expression in P/E. Together, our findings highlight the estrous cycle's ability to impact brain GLP-1R signaling and may have translational implications for timing of GLP-1RA administration across the ovarian cycle in premenopausal women. NIH-DK137443

P8
3:45

Dietary Protein Intake Is Negatively Associated With Energy Intake But Not With Body Mass Index In A Population-Based Norwegian Sample: The TromsÃ¸ Study 2015-2016 (Dorothy W. Gietzen New Investigator Awardee)

Rikke Eriksen[1], Kamilla Rognmo[1], Laila A. Hopstock[2], James E. McCutcheon[1]

[1]Department of Psychology, UiT The Arctic University of Norway, Tromso, Norway, [2]Department of Health and Care Sciences, UiT The Arctic University of Norway, Tromso, Norway

The protein leverage hypothesis proposes that the obesity epidemic is driven by the essential need to obtain sufficient dietary protein. In diets that contain low levels of protein, a leveraging mechanism will cause overconsumption of foods high in carbohydrate and fat as people attempt to reach their protein target. Ultra-processed foods (UPFs) may be involved in this process as they cause dilution of protein content in the western food supply. We investigated these phenomena using cross-sectional data from a large Norwegian population-based study, The Tromsø Study 2015-2016. We examined the relationship between dietary protein intake, total energy intake, body mass index (BMI), and the role of UPFs in a sample of inhabitants of the municipality of Tromsø, Norway (n = 11,152; 40-99 years; 53% women). Fitted power functions revealed partial protein leverage as indicated by a negative L-value (L = -0.36, p <.001), such that total energy intake decreased as the proportion of dietary protein increased. However - and contrary to the protein leverage hypothesis – the relationship between BMI and dietary protein was weak and positive (b = 0.01; p <.001), as tested with linear regression. Further, as the proportion of UPFs in the diet increased, dietary protein (%) decreased (b = -1.8; p <.001), while total energy intake (kJ) increased (b = 1,999; p <.001), a finding that supports the protein leverage mechanism. Finally, a high proportion of UPFs was related to a higher BMI (b = 0.01; p = .037), however, this effect was minimal. In summary, our study of middle-to-older aged Norwegians provides strong support for the protein leverage mechanism but no evidence for an effect of protein leverage on BMI.

Thursday, July 31, 2025

8:00 - 4:30 PM	Registration - South Mezzanine
Registration	

9:00 - 10:00 AM	North & South Mezzanines
Poster Session 4, Exhibits & Coffee Break	

Poster numbers 300-346 are located in the South Mezzanine. Poster numbers 347-384 are located in the North Mezzanine.

P301

Markers Of Glucose Homeostasis Are Associated With Attenuated Behavioral Flavor-Nutrient Learning In Humans

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In addition to orosensory mechanisms, post-oral signals of glucose metabolism are implicated in food learning, which could influence habitual eating patterns and body weight. Evidence suggests post-oral signaling is attenuated in obesity, potentially impacting food reward learning. Using pooled data from 2 pilot flavor-nutrient learning studies (n=11, n=15; body mass index [BMI]: 18-37 kg/m^2; hemoglobin A1c [HbA1c] <5.7%), we assessed whether markers of adiposity or glucose homeostasis were associated with post-oral reward learning. Flavors rated as similarly liked were paired with no calories (sucralose; CS-) or 75 calories (sucrose; CS+) in a drink. Participants consumed CS+ and CS- drinks 6 times each in randomized order. In a post-test, they rated liking and wanting for each previously paired flavor. BMI, waist-to-hip ratio (WHR), HbA1c, and fasting (≥4 hours) blood glucose (BG) and insulin were assessed. Linear mixed models were used to assess interactions between each biometric variable and drink condition on liking and wanting ratings. BMI and WHR were not associated with post-conditioning changes in ratings, but higher fasting BG ($t_{23.7}$=-2.32, p=0.03) and HbA1c ($t_{22.0}$=-2.29, p=0.03) were associated with attenuated changes in liking the CS+ compared to CS- flavor. In a subset (n=11), brain response to cued receipt of previously paired flavors was assessed with fMRI. HbA1c was positively correlated with greater activity in the medial prefrontal cortex (PFC; [-4, 58, 16], T=9.73), ventromedial PFC ([6, 46, -8], T=5.44), and caudate ([-10, 20, 4], T=5.70) in response to the visual cue preceding flavor delivery (CS+>CS-). These findings suggest glucose homeostasis may be an important moderator of flavor-nutrient learning, even among metabolically healthy individuals.

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Human Appetite Before And After A Meal Eaten Upon Waking From Cold-Sleep

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Long-duration spaceflight offers the chance to go further than ever before, but astronauts face many challenges during long missions. Cold-Sleep (CS) is a new protocol designed to address these challenges by slowing human metabolism via cooling for 20 hours/day. Inadequate nutrition is a major concern to astronauts yet the effect of metabolic manipulation on human appetite is unknown. We hypothesize that metabolic suppression during CS will impact participants' hunger (H), satiety (S), thirst (T) and desire-to-eat (DTE) scores before and after the waking meal.5 people (ages 43±15y, 80% male) experienced CS for 20 hours and waking activities for 4 hours. They ate a post-sleep meal, exercised for 1 hour, and ate a post-exercise meal. Both meals were *ad libitum*. The protocol was repeated for 5 consecutive days. Subjects rated H, S, T, and DTE using 100-cm visual analogue scales (VAS) pre- and post-meal. Post-sleep meal VAS were measured, scaled, and rounded to the nearest half millimeter. Statistical analyses were paired t-tests on pre-meal S, H, DTE and T on days 1 and 5; Pearson correlation assessed associations between pre-meal S and H.Pre-meal H, S, DTE, and T were not significantly different from day 1 to day 5: 27.4±20.9 and 38.1±5.7, 42.4±24.8 and 52.8±18.7, 48.5±25.7 and 61.0±22.5, and 75.1±17.2 and 63.3±12.1 respectively. H and S scores were positively correlated (r=0.68, p=0.0003) pre-meal and negatively correlated (r=-0.65, p=0.011) post-meal. Our data give a first look into the impact of metabolic manipulation on human appetite. Satiety is

disturbed upon waking from CS with a return to normal after eating. We will explore changes in satiety and examine the impact of meal composition on VAS scores.

P305 **Balancing A Low-Protein Diet : Can Weekly Protein Meals Prevent Increased Food Intake ?**

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Reducing animal protein sources in the diet is recommended to mitigate the environmental impact of food systems. However, reducing animal protein can lead to lower protein-to-calorie ratio which has been shown to result in increased energy intake and increased adiposity in animal models. Based on the protein leverage hypothesis, hyperphagia is a compensatory mechanism to get enough protein. We investigated whether switching from low-protein diet (10%) to high-protein diet (20%) once per week could prevent this increase in energy intake. Male Wistar rats (8 weeks old, n=32) were divided into 4 groups: 2 control groups fed 20% meat protein diet (P20) or 10% meat protein diet (P10), and 2 groups fed a basal 10% meat protein diet but presented with either a meat-based (P10+Meat) or plant-based (P10+Plant) 20% protein feed 1 day per week. All diets were isocaloric (protein replaced by starch in P10). Food intake and body weight were recorded daily. Body composition and circulating hormones (FGF21, leptin) and amino acids were assessed after 4 weeks. Rats on P10, P10+Plant and P10+Meat increased their food intake ($p<0.05$). Both treatment groups ate less on the high-protein days ($p=0.012$, $p=0.0003$), but intake rebounded once the basal diet resumed. Plasma FGF21 and adiposity increased in P10 rats compared to P20 rats ($p<0.0001$, $p=0.0157$), an increase that was blunted in P10+Meat and P10+Plant rats ($p>0.05$). Weekly high-protein diet, whether plant- or meat-based, was insufficient to prevent hyperphagia rebound, but it mitigated adiposity gain in rats fed a low-protein diet. Further studies are needed to better understand how protein feeding over time influences obesogenic risk and metabolic adaptations.

P307 **Ultra-Processed Food In The News: Effects Of Exposure To Public Facing Information About Ultra-Processed Vs. Nutrient-Focused Food Information On Sensory Ratings And Energy Intake**

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Ultra-processed foods (UPF) consumption is associated with negative health outcomes. There is now widespread mainstream media coverage of the UPF concept. Unlike traditional nutrient-focused public health messaging about foods of health concern, the UPF concept focuses on ‘unnatural’ processing and ‘artificial’ ingredients. Based on evolutionary psychology, this focus may evoke disgust responses and cause particularly pronounced consumer avoidance of such foods. In a pre-registered laboratory experiment we examined the impact on consumers of being exposed to public facing information about UPFs and compared this to public facing information about nutrient-focused information about foods. Participants (N = 96, 48M, mean BMI = 26) completed two sessions and in the second session were exposed to one of three matched articles: i) Outlining UPFs and the negative health outcomes linked to UPF consumption, ii) Outlining foods high in fat, salt or sugar (HFSS) and their negative health outcome, iii) Control article. Participants made sensory ratings (e.g., pleasantness, disgusting) and were given ad-libitum access to four foods of which two were both UPF/HFSS and two were both non-UPF/HFSS. Energy intake for both UPF/HFSS ($p = .832$, $\eta p^2 = .004$) and non-UPF/HFSS ($p = .396$, $\eta p^2 = .020$) foods did not differ between conditions, nor did ratings of disgust or pleasantness. Exposure to both UPF and HFSS articles did however increase concerns about consuming both UPFs and HFSS foods to a similar degree. Ultra-processing vs. nutrient-focused messaging about foods of health concern produce similar non-specific effects on self-reported consumer avoidance of highly processed and nutrient poor foods, but in the present study this did not affect sensory ratings of foods or energy intake.

P309 **Reward Value In Food Affects Stress Alleviation Via Food-Associated Reward Memory In Mice**

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Recent studies suggest a paradigm shift approach to alleviate anxiety by strengthening positive memories. Food-associated reward memory (FAR memory) has been shown to reduce anxiety-related behaviors in mice, but the role of food reward value remains unexplored. In this study, we hypothesized that FAR memory associated with high-reward-value food (HRV food) alleviates anxiety more effectively than standard food (STD food) in mice. In this study, the HRV food was developed with adding sugar and fat into the standard food. In Experiment 1, we examined whether FAR memory of the STD food affects anxiety-related behavior in mice. Twenty BALB/c and C57BL/6 mice were trained on the elevated plus maze (EPM) for 5 days. The results showed that FAR memory of the STD food alleviated anxiety-related behaviors in both species. In Experiment 2, we examined the reward value of foods using a runway test. The results showed that mice in the HRV food group showed higher running speed and more straight-line running than the STD food group.In Experiment 3, Forty mice were divided into HRV and STD groups to assess whether FAR memory of the HRV food alleviates anxiety-related behaviors better than the STD food memory. Mice were trained on EPM with either HRV or STD food cues for 5 days. Results showed that the FAR memory of the HRV food was more effective in alleviating anxiety-related behaviors than the STD food. In conclusion, the FAR memory associated with the HRV food is more effective in alleviating anxiety-related behavior compared to the STD food, providing insights into anxiety alleviation and stress-driven eating behavior.

P311 **The Effect Of Food Form And Child Sex On Energy Compensation For Apple Preloads**

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Research in adults has shown beverages produce less satiety than solid foods when matched for energy; however, less is known about the effect of food form on children’s energy regulation. We examined the effect of varying form of an apple preload on children’s short-term energy compensation (satiety). Children (n=64; mean age 5.9 years-old) completed a within-subjects, crossover study across 5 visits, each ~1 week apart. During each visit, children were presented in counterbalanced order with no preload (control) or one of 4 apple preloads: slices, purée, juice, or juice sweetened with non-nutritive sweetener. Apple slices, purée, and juice were matched for energy and energy density. Visual cues were masked and

eating rate was controlled by using an audiobook to cue children to consume a small portion of the preload. Following the preload, children ate *ad libitum* from a meal of common foods, and satiety was calculated as the % of energy intake at the preload + meal relative to meal intake in the no preload condition (100% = perfect compensation). Food form did not influence satiety, as percent compensation was 112%, 121%, and 120% for apple slices, purée, and juice ($p>0.05$). Results, however, varied by sex: boys showed near perfect (99%) compensation for apple slices and reduced subsequent meal intake ($p<0.01$), but no intake reduction was seen in girls. Across all preloads, boys showed better compensation than girls ($p<0.05$). Thus, when visual cues were masked and consumption rate was controlled, solid fruit and fruit juice had similar effects on satiety, but regardless of fruit form, boys showed better energy compensation than girls. Even in early childhood, satiety in girls may be driven more by social or learned cues while boys respond more to biological signals.

P315 **Modulating Food Ratings With Gamified Inhibitory Control Training**

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High Body Mass Index (BMI) is a risk factor for several diseases, such as diabetes and cardiovascular conditions. On a behavioral level, higher BMI is associated with low inhibitory control and high “wanting” for food rewards. This project investigates how food “wanting” can be modulated through inhibitory control training (ICT) in individuals with various BMI. We hypothesized a larger decrease in “wanting” for high-calorie foods after training in the experimental group compared to the control group.The ICT was gamified and personalized, reinforcing intrinsic motivation, engagement, and adherence to the intervention. Unlike most studies in the field that only provide a single training session, we trained participants for 200 minutes over 4 weeks, at home. We compared an experimental training group in which high-calorie foods were associated with motoric inhibition to an active control group in which both high- and low-calorie foods are linked with motoric inhibition. As the difference between the experimental and control training conditions lay only in the stimulus-response (SR) mapping proportions, both groups did the same task and had similar expectations. This control of participants’ expectations is another major asset of our approach. Preliminary results (n=51) do not show a significant interaction between intervention (experimental vs control training) and time (pre- vs post-intervention), $F(1, 51) = 2.8$, $p = .09$. The two intervention groups are currently still under a double-blind procedure. If we demonstrate that ICT can effectively reduce the valuation of high-calorie foods, it could provide easily implementable tools for weight management.

P317 **Evaluating The Impact Of Chronic Unpredictable Mild Stress And Binge-Like Eating Co-Exposure In Male And Female Rats.**

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Binge eating disorder, the most prevalent eating disorder in the USA, is frequently comorbid with depression, anxiety disorders, and substance use disorders. The present study evaluated the impact of chronic unpredictable mild stress (CUMS) and binge-like eating on overall caloric intake, body weight, and anxiety-like behavior in male and female Long Evans rats. Male and female groups of rats, matched for body weight, water, and food intake, were randomly divided into four groups (n=6/group) designated as chow (C), chow + stress (C+S), high-fat diet (H), and high-fat diet + stress (H+S). H and H+S groups of rats received intermittent access to a high-fat diet (HFD) on Mon, Wed, and Fri, whereas regular chow was provided to the C and C+S groups of rats. Following two weeks of such dietary exposure, rats in the stress groups were also exposed to chronic unpredictable mild stress (CUMS) randomly administered before HFD access over ten weeks. Food intake and body weight were recorded throughout, and finally, blood glucose and anxiety-like behavior were assessed using a glucometer and light and dark box, respectively. Intermittent HFD access induced binge-compensate feeding cycling in the H and HS group of male and female rats. While CUMS did not impact total caloric intake in any chow groups, it significantly reduced caloric intake in the HS compared to the H group of male rats only. The anxiety-like behavior was significantly increased in the male HS group only. Overall, no significant CUMS-related between-group differences in body weight and blood glucose levels were evident. Collectively, these data highlight the greater impact of combined binge-like eating and CUMS on overall caloric intake and anxiety-like behavior and related sex differences.

P319 **Exploring Sweet And Savoury Liking Status: Impact On Sensory Preference And Ad Libitum Intake Of Popcorn Snacks**

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Snacking contributes significantly to daily energy intake. While the effects of sweet and savoury tastes on satiation have been studied in a meal context, only limited research has been conducted in a snacking context. Sweet Liking Status (SLS), a measure of individual differences in sweetness preferences, may also influence snack intake as it impacts food preferences. Savoury Liking Status (SavLS) remains understudied, with no validated method for its measurement. This study piloted a novel method to screen SavLS and investigated the relationships between SLS and SavLS, and their influence on liking, emotional responses, and ad libitum intake of sweet and savoury popcorns. In Session 1, participants (n=80) evaluated popcorns; one sweet, one salty and three savoury (spiked using nutrition yeast to have different savoury intensities). SLS classification was measured following the 3-solution method of Kavaliauskaite et al. (2023) and SavLS classification was done through AHC cluster analysis using the savoury popcorn variants. Next, participants completed two ad

libitum intake sessions (one each with sweet and savoury popcorn) and ad libitum consumption was measured (weight, calories, eating rate). Results showed that the savoury popcorn variants successfully grouped participants into High, Medium and Low Savoury Likers. The results on the association between SLS/SavLS, and how SLS/SavLS impact on liking, emotional response and intake of sweet and savoury popcorns will be reported. Ã¢Â€Â¯The methodology established here paves the way for future research into SavLS, provides insights into snacking behaviour and has broader implications for dietary behaviour and personalised nutrition strategies.

P321 **Blocking Sweet Taste Perception With Gymnema Sylvestre: Characterizing The Time Course And Variability.**

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Despite their widespread use to mitigate metabolic risks, the effects of artificial sweeteners (AFSs) on obesity and diabetes remain unclear. AFSs bind to sweet taste receptors, transmitting signals to the brain via presynaptic cells and cranial nerves. These receptors are also found in extra-oral tissues, including the brain and gut, where they may influence metabolism (Laffitte et al., 2014). A key study found that consuming sucralose with, but not without, carbohydrates reduced insulin sensitivity and decreased midbrain, insular, and cingulate responses to sweet taste (Dalenberg et al., 2020), though mechanisms remain unclear. This study examines the role of oral and post-oral sweet taste receptors in AFS effects on metabolism. While previous research suggests Gymnema Sylvestre (GS) blocks sweet taste for up to an hour, little is known about the exact time course or individual variation in its effectiveness. To address this, we developed a protocol for sweet taste receptor blockade using GS. Ten healthy participants rated the sweetness of a flavored beverage before and after rinsing with GS tea. Sweetness intensity was measured using the general labeled magnitude scale (Green et al., 1996) at baseline and every 5 minutes post-rinse, continuing until ratings were within 5 points of baseline (100-pt scale). Repeated measures ANOVA showed that ratings at 5, 10, and 15 minutes post-rinse differed significantly from baseline. However, blockade duration varied widely, lasting from 0 to 100 minutes. Results confirm GS effectively blocks sweet taste but suggest highly variable duration across individuals.

P323 **The Role Of Depression, Dietary Restraint, And &Ldquo;Food Addiction&Rdquo; In The Association Between Premenstrual Symptoms And Disordered Eating: Preliminary Findings**

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Severe premenstrual symptoms have been linked to disordered eating, such as binge eating and emotional eating, as well as weight preoccupation and addictive behaviors. The purpose of this study was to examine variables that may explain the association between premenstrual symptoms and disordered eating. We collected responses to the Premenstrual Symptom Screening Tool (PSST), risk for eating disorder (SCOFF), depression (DEP), dietary restraint (DR), emotional eating (EE), external eating (ExE), and food addiction (FA) from 600 women aged 18-35 years (M=26.6, SEM=.21) with a mean body mass index (BMI) of 26.5 (SEM=.40). 45.5% had a BMI≥25. Purposive sampling was employed to acquire equal numbers of Asian, Black, Latina, and White participants. PSST was positively correlated with DEP (r=.38), ExE (r=.33), DR (r=.35), EE (r=.41), FA (r=.43), and SCOFF (r=.34), all p<.001. SCOFF was significantly correlated with DEP (r=.30), ExE (r=.22), DR (r=.33), EE (r=.40), and FA (r=.55), all p<.001. BMI was not associated with PSST or SCOFF in bivariate correlations. Linear regression showed that, of these, PSST (β=.08), DEP (β=.10), DR (β=.10), EE (β=.11), and FA (β=.40) were significant unique contributors to SCOFF (controlling for BMI), adjusted R^2=.33. A parallel mediation model showed that the relationship between PSST and SCOFF was fully mediated by DEP (b=.005, 95%CI: .002-.008), DR (b=.004, 95%CI: .001-.007), and FA (b=.020, 95%CI: .015-.026), but not EE (b=.003, 95%CI: .-001-.007), F(7,592)=43.09, p<.0001, R^2=.34. These results suggest that severe premenstrual symptoms increase risk for disordered eating via elevated depression, uncontrolled eating in the form of FA, and attempts to control consumption in the form of dietary restraint.

P325 **Juvenile Exposure To A Bitter Diet Increases Acceptance Of Quinine In Adulthood**

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Repeated exposure (RE) is an effective method to increase acceptance of healthy, often bitter, vegetables in children. Whether the increased acceptance after RE persists long-term and into adulthood is unknown. The standard protocol in our lab is to use repeated exposure to a bitter diet to increase salivary protein (SP) expression in adult rats. These SPs decrease bitter taste sensitivity and increase bitter acceptance. Here, we ask whether juvenile exposure to a bitter quinine diet increases bitter acceptance in adulthood. To do this, pups were weaned at postnatal day (PD) 21 onto a 0.375% quinine diet or a control diet. After 14 days of quinine diet exposure, quinine-fed rats were switched to the control diet for the remainder of the study. At adult-onset (PD 65), half of the rats were tested in brief-access taste tests while the other half were given long term acceptance tests. Brief-access animals were offered various concentrations of sucrose and quinine in separate tests. There was no effect of early life exposure on responding to either stimulus (p's > 0.05). Long term test rats were given 22-hr access to a bottle of 1mM quinine solution. Intake was measured at 6-hr and 22-hr timepoints. Quinine-exposed rats (n=5) show greater quinine intake at 6 hrs compared to control (n=5, p = 0.07). Quinine-exposed rats also show increased burst number to quinine (p = 0.07) but no differences were observed in burst size. These data suggest that early-life exposure

to bitters can increase acceptance of bitter into adulthood. We are also collecting saliva samples across the lifespan to determine if this long-term change in acceptance is related to salivary protein change.

P327 **Genetic Sequence And Knockout Studies Implicate A Role For *Rgs7Bp/Rgs7Bp* In Obesity**

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Obesity affects 108 million U.S. adults. Current medications require ongoing use, have side effects, and warrant new drug targets. Here, we report a link between the gene encoding regulator of G protein signaling 7 binding protein (RGS7BP) to obesity. In GWAS, *RGS7BP* variants associate with BMI (15 studies), body weight (BW), smoking, and chronotype. In the Levin polygenic rat model of vulnerability to high-fat-diet-induced obesity (DIO, n=23), *Rgs7bp* is under-expressed in the ventromedial striatum (Log2FC=-0.850; p<.0001) and highly mutated vs. diet-resistant (DR, n=35) and reference genome. GATK HaplotypeCaller identified 263 high-quality position calls for DR and 431 for DIO. Of 103 polymorphisms with sufficient DIO and DR calls for comparison, 52 were more frequent in DIO than DR (Odds ratios 9.11-175.67, all p<0.05), with none more common in DR. To assess a causal role for *Rgs7bp*, we study BW/composition and chow (Teklad 2018) intake of *Rgs7bp* knockout mice (KO; n=11) and wildtype (WT; n=15) at weekly intervals from P21. So far, at P35, a Genotype main effect reveals KO mice are fattier than WT. At 8 weeks, mice will be single-housed and provided ad libitum 5TUM chow (TestDiet; 3.30 kcal/g; 10.4% fat) for 2 weeks via FED3 devices, then randomly assigned to receive: 1) continuous 5TUM, 2) continuous sweet-fat diet (more preferred, 35% fat, 31% sucrose [kcal]; 4.18 kcal/g; Bio-Serv), or 3) intermittent sweet-fat (24h, 3d/wk) with 5TUM on non-access days. Intake, BW/composition, meal pattern, chronotype, and operant performance will be compared across genotypes and diets. We hypothesize KO mice will remain fattier and consume more, gain weight, and exhibit heightened early-dark-cycle-onset feeding, especially in continuous and intermittent sweet-fat diet conditions.

P329 **Hypothalamic Ensembles Driving Maladaptive Behaviour In The Activity-Based Anorexia Model**

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Anorexia nervosa (AN) is an eating disorder characterized by a fear of weight gain, low body weight, and hyperactivity, with a mortality rate among adolescent patients higher than that of any other mental disorder, and lacking biology-based therapies. We hypothesize that neurons affected by changes in energy balance related to AN will reveal potential targets for novel therapies. In this study, we used 128 TRAP2 mice, in which 2A-iCreER^{T2} is knocked into the Fos locus to create a cue-dependent neuron labeling system, to investigate neuronal ensembles involved in the Activity-Based Anorexia (ABA) model. Specifically, we aimed to identify neurons active during the food-anticipatory phase of the ABA model, in which nocturnal mice exhibit excessive wheel running during the light phase despite a strong negative energy balance—a marker of AN-like behavior. Mice exposed to the ABA model showed a significantly higher number of labeled neurons in several hypothalamic regions compared to controls (5 groups, n = 7-8 each, p <0.05, using a one-way ANOVA followed by Dunnett's post-hoc test). We characterized these neurons using single-cell RNA sequencing (3 groups, n = 3 each) and immunohistochemistry (ABA group, n = 6). Chemogenetic modulation (3 groups, n = 11-16 each) of these neuronal ensembles, such as those in the dorsomedial hypothalamus, allowed us to dissect their role in anorexic behaviors. These alterations in neuronal activity identify hypothalamic ensembles that are central to AN-like behaviors, particularly hyperactivity, which contributes to disease onset and severity. Our findings highlight the potential of hypothalamic ensembles as drivers of AN pathophysiology and as targets for developing more effective treatments.

P331 **Single Nuclei Transcriptomic Atlas Of The Human Dorsal Vagal Complex**

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The dorsal vagal complex (DVC)—comprising the area postrema (AP), medial and lateral nucleus of the solitary tract (mNTS, lNTS), and the dorsal motor nucleus of the vagus (DMX)—is a critical brainstem hub for integrating visceral sensory inputs and regulating autonomic and ingestive behaviors. While rodent studies have advanced our understanding of the DVC, the molecular organization of this region in the human brain remains poorly defined. Here, we present the first single nuclei RNA sequencing (snRNA-seq) analysis of the human DVC using postmortem brainstem tissue from both male and female donors. By profiling high-quality cellular nuclei across the AP, mNTS, lNTS, and DMX, we identified distinct cell type clusters, including transcriptionally defined subtypes of excitatory and inhibitory neurons unique to each DVC subregion. Notably, we found region-specific expression patterns of neuropeptides, receptors, and transcription factors implicated in appetite regulation, autonomic control, and neurodegenerative disease. These molecular fingerprints reveal substantial interregional transcriptional diversity within the human DVC. This work provides the first comprehensive atlas of human DVC cellular composition and gene expression, offering a foundational resource for translational research on feeding, metabolism, and autonomic regulation in humans.

P333 **Brainstem Bdnf Neurons Are Downstream Of Gfral/Glp1R Signalling**

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Growth differentiation factor 15 (GDF15) reduces food intake, delays gastric emptying and induces nausea, aversion and metabolic adaptation, effects that are similar to those of glucagon-like peptide-1 receptor agonists (GLP1RA) administered systemically. GDF15 signals exclusively through its receptor, GFRAL, located only in the area postrema and nucleus of the tractus solitarius (AP/NTS) of the brainstem. While GFRAL neurons are known to mediate the aversive effects of GLP1RA, their role in metabolic adaptation remains unclear. Importantly, GDF15 treatment reduces obesity not only by suppressing appetite but also by counteracting the compensatory reductions in energy expenditure observed upon caloric restriction. Using a chemogenetic model, we demonstrate that selective GFRAL neurons activation is sufficient to mimic the anorexigenic effects of GDF15 and to significantly reduce body temperature, energy expenditure and respiratory exchange ratio (RER). In addition to the characterised aversive pathway via the parabrachial nucleus, we identify a population of brain-derived neurotrophic factor neurons in the medial NTS ($BDNF^{mNTS}$) downstream of GFRAL cells. By disabling these neurons or knocking down brainstem *Bdnf* expression, we have shown that these neurons are crucial for the acute weight-reducing effects of GDF15 and the GLP1RA, Exendin-4, as demonstrated by attenuated responses in body weight, food intake and RER. Furthermore, selective activation of $BDNF^{mNTS}$ neurons using a chemogenetic model was sufficient to reduce food intake and drive fatty acid oxidation, suggesting that these neurons may serve as a promising target for therapeutic interventions in obesity and diabetes treatment.

P335 **Sex Differences In Drinking Patterns And Microstructure During Voluntary Adolescent-Onset Ethanol Intake And Subsequent Brain-Wide Cfos Activity During Forced Ethanol Abstinence**

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Adolescent alcohol use increases the risk of developing alcohol use disorder (AUD), with negative affect during abstinence heightening relapse risk. This study aimed to analyze ethanol drinking patterns and microstructure and brain-wide neural changes during abstinence in male and female mice with adolescent-onset ethanol consumption. Adolescent C57BL/6J mice (~PND30) were placed into the Lick Instance Quantifier (LIQ) system with two bottles containing ethanol and water or both water as controls. Mice underwent the Chronic Drinking Forced Abstinence paradigm with continuous access to the bottles and precise measures of drinking behavior, including lick count, duration, bout number, and bout size, were monitored throughout. While there were no major sex differences in total licks at the ethanol bottle, females exhibited higher bout numbers compared to males. Additionally, the timing of drinking relative to dark onset differed, with females drinking more before dark onset and males drinking more immediately after dark onset. Ethanol was then removed, and brains were collected at 24hrs and 2wks of forced abstinence. Brain tissue was cleared, immunostained for cFos, and imaged using light sheet microscopy. Brain-wide cFos densities were analyzed for regionally specific changes and related to drinking behaviors. Hierarchical clustering and network analysis showed decreased network modularity during acute withdrawal, with a return to higher modularity during protracted abstinence. The combined LIQ and whole brain cFos data within the same animals offers insight into neural mechanisms underlying the development of negative affective behaviors during abstinence and their relationship to drinking behavior in adolescence.

P337 **Sex Differences In Uncertainty-Driven Food-Seeking Behavior And Orexin Reward Effects**

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Uncertainty in food access increases food-seeking and obesity with larger effects in women compared to men, yet the biological mechanisms of these effects remain poorly understood. We modeled uncertainty in sustenance food (food required to fulfill caloric needs, SF) in male and female C57BL6 mice by using either unpredictable or predictable pellet delivery (pellets were delivered with a random or constant delay on weekdays; all mice had free pellet access on weekends, n=6/group/sex). After 8 weeks, SF uncertainty reduced body weight gain by 2.8±0.89% (P=0.02) and food intake by 9±0.4% (P=0.05) in females without effects in males. Only in females, uncertainty increased by 181±47% the attempts to retrieve pellets (P=0.01), but increased the speed of pellet retrieval in male and female mice (females:64.9±18.2%; males:77.3±18.2%; P<0.01). Next, mice (n=4/group/sex) were implanted with a cannula aiming at the right ventral tegmental area (VTA) and trained to consume sweet-condensed milk (SCM) in FR5 and demand curve (DC) schedules. During FR5, and compared to control conditions, SF uncertainty increased SCM intake by 90.5±35% only in females (P=0.02). During DC, SF uncertainty increased decreased demand elasticity for sucrose in SF uncertainty males across all OXA doses compared to control males (62±26.9%, P=0.04) and OXA decreased demand flexibility in control male mice, reaching similar levels to those of males exposed to SF uncertainty. SF uncertainty or OXA in VTA did not alter SCM intake, demand parameters on females or demand intensity on males. We

are currently increasing sample size for these experiments, yet these data suggest different behavioral adaptations to uncertainty in males and females to both sustenance and palatable food and that SF uncertainty enhances behavioral effects of OXA in VTA among male and not female mice.

P339 **A High Saturated-Fat Diet Enhances Microglial Activation Proximal To Dopamine Terminals In The Nucleus Accumbens Of C57Bl/6J Mice.**

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Premise: Saturated fatty acids are known to activate microglia. We investigated whether this activation and the resulting inflammation affect dopamine neurotransmission in the nucleus accumbens (NAc). **Hypothesis:** A high-fat (HF) diet would enhance microglial activation measured by immunohistochemistry (IHC), and impair dopamine terminal function, assessed via dopamine release and uptake kinetics. **Species:** Male (n=56) and female (n=56) C57BL/6J mice were fed control (CN), medium-fat (HF30), or high-fat (HF60) diets. Mice were randomized for IHC to assess microglial activation or fast-scan cyclic voltammetry to measure dopamine. Subsets received anti-inflammatory (ketoprofen) or pro-inflammatory (lipopolysaccharide, LPS) treatments before IHC or voltammetry. **Results:** Increasing dietary saturated fat enhanced microglial activation near dopamine terminals in the NAc, shown by elevated Iba1 expression, a marker of pro-inflammatory microglia. Ketoprofen reduced this activation in HF-fed mice and attenuated the IL-6–induced reduction in dopamine release. This suggests HF-induced microglial activation sensitizes dopamine terminals to cytokines. Notably, chronic low-dose LPS administered via subcutaneous minipump in CN mice neither activated microglia nor altered dopamine kinetics after cytokine exposure. **Conclusions:** A HF diet promotes a pro-inflammatory state in the NAc, activating microglia and enhancing cytokine-induced dampening of dopamine signaling. These effects may contribute to disorders involving dopamine system dysregulation.

P343 **Inflammation-Induced Anorexia: The Sensory Afferent Pathways By Which Interleukin-1B Suppresses Agrp Neuron Activity And Appetite**

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Gut-brain communication plays a central role in appetite regulation, and how this is disrupted during sickness is incompletely understood. Here, we explore how inflammation modulates the activity of hunger-promoting AgRP neurons, a critical central target for feeding related sensory stimuli. Our findings show that the inflammatory cytokine interleukin-1β (IL-1β), which is elevated across a broad range of diseases that affect appetite and energy balance, including acute infections, autoimmune diseases and cancers, inhibits AgRP neurons on a time frame consistent with its induction of anorexia. IL-1β-induced AgRP neuron inhibition is entirely dependent upon prostaglandin synthesis, though IL-1β-induced anorexia is only partially prostaglandin-dependent suggesting multiple circuits and molecular pathways through which this cytokine impacts appetite. Using chemogenetic approaches, we have shown that IL-1β- and prostaglandin-induced feeding suppression requires the activity of peripheral sensory neurons, in particular spinal afferents. Taken together, this project has begun to unravel how acute inflammation modulates the activity of canonical feeding circuits to drive sickness behaviors including anorexia. Future work will focus on further clarifying the contributions of vagal versus spinal sensory signaling to inflammation-induced anorexia, and on determining molecular mediators of this response beyond prostaglandins.

P345 **Sex Differences In Pavlovian Outcome Devaluation Implicate A Differential Role Of Orexin Signaling In Male And Female Rats**

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The motivation for rewards depends on both the outcome value and associated environmental cues that predict the outcome's availability. When the outcome value decreases, some individuals decrease conditioned behavior to the associated cues and outcomes, while others persist in their behaviors. This behavioral inflexibility due to learned cues contributes to addiction, overeating, and other maladaptive behaviors, and importantly, sex differences are evident in these behaviors. The neuropeptide orexin/hypocretin (ORX) is involved in motivation, learning, and addiction, and previous research has shown sex differences in the ORX system. Using specific satiety-induced outcome devaluation, we examined sex differences and the role of ORX in behavioral flexibility. We trained Long-Evans rats on Pavlovian conditioning (a novel cue (i.e. tone, lever) predicts palatable food pellets). Then we sated rats on either the training pellets (Devalued condition) or an equally caloric outcome (Valued condition), counterbalanced across two test days, and presented rats with the cue alone to examine cue motivated behaviors independent of outcome delivery. Males reduced responding during the cue under Devalued compared to Valued condition (n=28; $p<0.001$), while females did not (n=28, $p=0.23$), suggesting females are less sensitive to outcome devaluation potentially due to heightened ORX signaling. To block ORX signaling, we microinjected the ORX 1 receptor antagonist SB-334867 (SB) into the ventral tegmental area and observed restoration of devaluation sensitivity in females (n=5 SB, n=4 vehicle; $p=0.07$), but no change in males' sensitivity (n=4 SB; n=3 vehicle). These findings indicate differential ORX signaling between males and females that underlie differences in behavioral flexibility.

P347 **Amylin Receptors On Serotonin Neurons: A Link Between Emotionality And Weight Regulation**

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Amylin, a peptide hormone secreted by the pancreas in response to food intake, is gaining attention as a potential treatment for obesity, with its analog pramlintide already approved for use in type 1 and type 2 diabetes. The serotonin system is a key regulator of emotionality and metabolism. Various serotonin receptor agonists have been approved as weight loss pharmacotherapies, but adverse side effects have led to their market withdrawal. Using fluorescent in situ hybridization, we found that amylin receptor components are present on serotonergic neurons in the dorsal raphe (DR), a serotonin hub in the forebrain. This suggests amylin may exert part of its anorexic effect via engaging the serotonin system; however, the functional relationship between these two systems regarding food intake control remains poorly understood. To determine if brain serotonin signaling is necessary for amylin's anorexic effects, we tested whether pharmacological blockade of 5HT2A or 5HT2C interacts with the reduced food intake produced by brain-applied amylin in male and female rats. We found that intracerebroventricular amylin induced a robust anorexic response in both sexes. This chow intake reduction was attenuated by blockade of the 5HT2C receptor in female rats (n=12), but not male rats (n=12). Blockade of the 5HT2A receptor did not affect amylin anorexia in either sex. These findings indicate that serotonin mediates amylin anorexia in a sex-divergent manner. Targeting the amylin system may offer a refined way to engage the appetite-reducing properties of the serotonin system for anti-obesity therapy, avoiding broader serotonin system activation side effects.

P349 **Glucose-Dependent Insulinotrophic Polypeptide Regulates Food Intake And Body Weight Via The Area Postrema In Mice**

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The development of dual agonists for the glucagon-like peptide-1 and glucose-dependent insulinotrophic polypeptide receptor (GLP-1R and GIPR respectively) is a landmark moment in the treatment of type 2 diabetes and obesity. In preclinical and clinical studies, GLP-1R-GIPR co-agonism improve glycemia and reduce body weight superior to GLP-1R agonism alone, however the role of GIPR agonism remains incompletely understood. Evidence suggests that long acting GIPR agonists act in the CNS to reduce food intake and body weight via an inhibitory GABAergic neuronal population. Here we demonstrate that peripherally administered acyl-GIP decreased food intake in lean mice ($n = 6$ per treatment, $p<0.05$ by two-way ANOVA). This effect was abolished in mice with deletion of GIPR in the area postrema (AP), utilising $GIPR^{flox}$ animals and an AAV-Cre ($GIPR^{DAP}$, $n = 8$ per group, $p<0.05$ by two-way ANOVA). As the AP, a component of the hindbrain's dorsal vagal complex which lies at the caudal end of the brainstem and integrates sensory information from the gastrointestinal tract, has been implicated in both food intake control and aversive responses, we further investigated the ability of Acyl-GIP to counteract flavour-avoidance. $GIPR^{WT}$ and $GIPR^{DAP}$ mice avoided flavours paired with PYY, which could be prevented by treatment with acyl-GIP in $GIPR^{WT}$ but not $GIPR^{DAP}$ mice ($n = 6$-10 per group, $p<0.01$ by one-way ANOVA). Finally, $GIPR^{DAP}$ mice were protected from weight gain following high fat diet feeding, consistent with the global GIPR KO mouse model ($n = 4$-6 per group, $p<0.01$ by two-way ANOVA). Our data demonstrate that long acting GIPR agonists depend on GIPR signalling in the area postrema to decrease food intake and body weight.

P351 **Increased Insular Responses To High-Calorie Versus Low-Calorie And Neutral Images After Tetrahydrocannabinol (Thc) Administration**

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Introduction: The endocannabinoid system (ECS) is a neuromodulatory system that exerts an energy-stowing function. While preclinical and indirect human evidence suggest a key role in food reward, direct causal evidence remains limited. We aimed to investigate the effects of pharmacological stimulation of the ECS on food reward. Methods: A double-blind, cross-over fMRI study was performed in 13 healthy participants. Before scanning, 1.25 mg of tetrahydrocannabinol (THC), a cannabinoid receptor type 1 agonist, or placebo was administered intravenously. During scanning, participants viewed high-calorie food, low-calorie food or neutral images and provided liking, wanting and pleasantness ratings. Imaging data were analyzed with general linear models, ratings with linear mixed models. Results: Whole-brain parcel-wise analysis showed greater activation for high-calorie versus neutral images in the THC compared to placebo condition in the left anterior (max $Z=5.3767$) and right inferior insula (max $Z=7.0345$). Region-of-interest analysis showed increased activation for high-calorie images versus low-calorie and neutral images in the THC compared to placebo condition in the bilateral posterior insula (left: $p=0.01$, right: $p<0.001$).No significant differences were found in voxel-wise analyses in a mask of reward regions. Higher wanting and liking ratings were found for high-versus low-calorie images (both $p <0.001$), while pleasantness ratings were higher for high- and low-calorie images compared to neutral images ($p<0.001$). There was no significant effect of condition nor condition-by-image type interaction on ratings. Conclusion: THC administration increased insular responses to high-calorie food cues but did not affect ratings.

P353 **Differential Phasic Dopamine Responses Develop As A Function Of Experience With Metabolically Distinct Access To Sugars**

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Phasic activity of the mesolimbic dopamine system plays a role in encoding the value of food and food-directed motivation. The value of food fluctuates with physiological state, post-ingestive consequences and learning. For example, experience

with the metabolically distinct sugars glucose and fructose enhance preference for the orosensory properties of glucose. Here, we tested the hypothesis that such experience would modulate the phasic dopamine responses to voluntary consumption of these two sugars. We expressed the fluorescent dopamine sensor GRAB_DA3m in the nucleus accumbens of rats and measured phasic dopamine signaling using in vivo fiber photometry. Upon recovery, rats were habituated to the availability of a drinking spout for 30min sessions. Then, in separate sessions, 0.56M glucose or 0.56M fructose was made available in semi-randomized order (such that no sugar was available for more than 2 consecutive sessions). Most investigations of phasic dopamine signaling occur in brief and structured trials rather than during self-paced voluntary consumption. We measured dopamine responses relative to defined microstructural analyses including the onset of bursts and clusters. Aligning dopamine signaling to the onset of licking, we found similar dopamine responses for both sugars the first time each was presented. By the second presentation, though, the dopamine response to glucose was dramatically potentiated and substantially higher than that to fructose. The findings suggest that phasic dopamine release tracks the experience-dependent valuation of sugars.

P355 **Modeling Effects Of Early Life Food Insecurity In Rodents On Reward Systems And Metabolic Health**

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Unpredictable access to food during the critical period of adolescence disrupts development, increasing the risk of metabolic dysfunction and behavior deficits. While adverse consequences of food insecurity have been shown in humans, rodent models allow greater control to assess them. The mesolimbic dopamine system has a critical role in modulating reward sensitivity and is affected by food restriction and inconsistent eating. Stimulation of the medial forebrain bundle (MFB) using intracranial self-stimulation can assess changes in reward sensitivity. We modeled food insecurity in adolescent rats (n=16) with a pseudorandomized feeding schedule, where insecure rats received 4 meals, one randomly omitted, alternating between 75% and 125% of 90% ad lib intake, and secure rats received 4 meals at 90% daily intake of age-matched rats. Body weights were measured across the study. Blood glucose was measured after a 16hr fast then at intervals of 0 to 120 mins post glucose solution intake. Measurements were done before and after an 8-day high-fat, high-sugar (HFHS) diet challenge. Preliminary data shows greater body weight gain in food insecure females and suggests impaired glucose tolerance following HFHS challenge. In adulthood, rats were implanted with a bipolar electrode in the MFB and trained to self-administer stimulation across a range of frequencies to determine minimal frequency (alpha) supporting maximal administration. We then measured how well rats discriminate “small” and “large” rewards (95% vs 25% of alpha). Finally, rats completed a delay discounting task where the delay for the “large” reward was increased to assess impulsivity. The effect of food insecurity on impulsivity and reward processing in adulthood will be assessed.

P357 **Determining The Effects Of Glp-1R Activation On Cerebellar Synaptic Transmission.**

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The gut hormone glucagon-like peptide 1 (GLP-1) is a key contributor to the control of food intake and reward processing. GLP-1 receptors (GLP-1R) are widely expressed throughout the central nervous system where their signaling alters neuronal excitability to suppress intake and the rewarding effects of food. Recent studies have shown GLP-1R expression in Purkinje cells (PCs) within the cerebellum, a region gathering increasing appreciation for playing a role in reward processing. Importantly, the cerebellum responds to feeding signals and directly projects to key mesolimbic nuclei that initiate appetitive behaviors, including food intake. What remains unclear is whether GLP-1Rs are expressed in other cell types of the cerebellar cortex and how their activation modulates synaptic transmission and potentially feeding. Here we combined RNAscope and immunohistochemistry with electrophysiology to map GLP-1R expression and signaling across different cell types of the cerebellar cortex. We saw that in addition to its known expression in PCs, GLP-1Rs are densely expressed in the granule cell (GC) layer, likely in both GCs and innervating mossy fibers, across all lobes of the cerebellar cortex. Bath application of the GLP-1R agonist exendin-4 increased the frequency of spontaneous excitatory post synaptic currents in the majority of GCs and increased PC action potential firing, consistent with direct actions on PCs or increased excitatory synaptic drive from upstream GCs.This previously uncharacterized response of GCs to GLP-1R activation strongly supports the ability of the cerebellum to integrate viscerosensory signals and provides an expanded understanding of neurobiological targets responsive to GLP-1 signaling, which may contribute to the control of excessive food intake.

P359 **Fluorescent Glp1R/Gipr Dual Agonist Probes Reveal Cell Targets In The Brain**

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The advent of dual incretin agonists, targeting both the glucose-dependent insulinotropic polypeptide receptor (GIPR) and glucagon-like peptide-1 receptor (GLP1R), represents a key advance for incretin-based pharmacology. Expression of *Gipr* and *Glp1r* in the central nervous system is critical for incretin-induced weight loss. However, the cellular substrates through which incretins act centrally to reduce body weight are not fully understood. In this study we characterized daLUXendin, a novel fluorescent GLP1R/GIPR dual agonist probe developed to help delineate cell targets of dual incretin agonists. To confirm that daLUXendin is a functional GLP1R/GIPR dual agonist, we first assessed its in vivo potency. Peripheral administration of daLUXendin decreased food intake over 12 hours in mice through potently decreasing meal number. To explore the central targets of daLUXendin, we dosed mice with intravenous or intracerebroventricular daLUXendin. Using immunohistochemistry and RNAscope, we found that daLUXendin principally localized to circumventricular organs (CVOs) and bound GLP1R+ and GIPR+ neurons in both the area postrema and the arcuate nucleus, as well as cell bodies and processes of tanycytes lining the third ventricle. daLUXendin additionally labelled the posterior pituitary, a key projection site of axons originating from GIPR neurons in the paraventricular nucleus of the hypothalamus. These data both validate the new fluorescent GLP1R/GIPR dual agonist, daLUXendin, and add to the characterization of cell types accessed

by dual incretin agonists. Future work is needed to define a role for the diverse cell types targeted by dual agonists in mediating the effects of incretin-based pharmacology on the regulation of body weight and food intake.

P361 **Functional And Anatomical Circuit Characterization Of Brainstem Ppg Neurons**

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GLP-1 producing preproglucagon (PPG) neurons in the brainstem project to multiple areas throughout the brain where they store and release GLP-1 from axons. PPG neuron activation has been linked to numerous functions, including food intake suppression. PPG neurons are located in the nucleus tractus solitarius (NTS) and the intermediate reticular nucleus (IRT), and even though these cell population project to similar targets, it is unclear how homogeneous these populations are. Considering how GLP-1 shows differential effects depending on where in the central nervous system it is injected, it is plausible that the PPG neurons similarly elicit site-dependent effects and could therefore be separated into subgroups. Here we aim to characterize the functional connectivity of PPG neurons. We chemogenetically activated NTS PPG neurons unilaterally in a Glu-venus mouse model and then quantified cFos immunoreactivity in PPG neurons ipsi- and contralateral to the activated PPG neurons. The number of cFos+ neurons was substantially higher in chemogenetically activated neurons compare to controls. However, there was no significant increase of cFos+ PPG neurons in the contralateral NTS, nor in ipsi- or contralateral IRT. Furthermore, we used these mice to investigate cFos immunoreactivity in forebrain areas with PPG projections and compared the ipsi- and contralateral hemispheres. Finally, retrograde AAV was injected unilaterally into different forebrain areas of PPG-cre mice to assess the specific subset and their spatial distribution of neurons projecting to these injection site. Overall, our results indicate distinct circuits, providing evidence for PPG neuron heterogeneity.

P363 **Orexin Population Activity Precisely Reflects Net Body Movement Across Behavioral And Metabolic States**

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Tracking net body movement in real time may enable the brain to estimate ongoing demands and thus better orchestrate muscle tone, arousal, and homeostatic energy balance. The identity of neural populations interfacing movement with internal metabolism remains unclear. In this study, we compared self-initiated movement-related activity in genetically-defined subcortical neurons across the mouse brain, including dopaminergic, glutamatergic, noradrenergic, and key peptidergic (hypocretin/orexin, SF1) neurons. We show that glucose-sensing hypocretin/orexin-producing neurons (HONs) in the lateral hypothalamus are exceptionally precise movement-trackers (n = 15 mice). Using a deep learning behavioral classifier, our data shows HONs encode net body movement across multiple behavioral states with a high degree of precision. Furthermore, we found HON movement tracking was robust across internal energy states, and occurred in a communication bandwidth distinct from HON encoding of blood glucose. At key projection targets, hypocretin/orexin peptide outputs correlated with self-initiated movement in a projection-specific manner, indicating functional heterogeneity in HON outputs. In contrast, we found that body movement was not encoded to the same extent in other key neural populations related to arousal or energy. These findings indicate that subcortical orchestrators of arousal and metabolism are finely tuned to encode net body movement, constituting a bridge multiplexing ongoing motor activity with internal metabolic resources.

P365 **Lateralized Expression Of Cholecystokinin Receptors In Nodose Ganglia Of Rats**

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The vagus nerves transmit sensory information from the gut to the brain, regulating feeding and energy homeostasis. Gut-innervating vagal afferents exhibit lateralized activation of midbrain “reward” circuitry, with projections through the right, but not the left, vagus nerve driving reward-related behaviors and dopamine release. However, the extent to which differential gene expression in vagal sensory neurons contributes to this asymmetry remains unknown. Using single-nucleus RNA sequencing, we compared gene expression in the left and right nodose ganglia (NG) of naïve rats. We identified a cluster of neurons co-expressing *Chrna3* (nicotinic acetylcholine receptor subunit 3) and *Cckar* (cholecystokinin A receptor, CCKAR) preferentially expressed in the right NG of rats (n=36; GSE280062; Bonferroni-corrected binomial tests). A similar right-biased cluster was also identified in a publicly available mouse dataset (n=6; GSE185173). RNA fluorescence in situ hybridization confirmed a right-bias of *Cckar*+ neurons in rats (n = 6) and mice (n = 6) (paired t-tests). CCKARs in gut-innervating NG neurons regulate satiety, macronutrient sensing, and nutrient preference. Thus, right-biased expression of *Cckar*+ NG neurons is a strong candidate for driving lateralized vagal reward-related signaling. We further examine functional differences in the roles of the right and left vagus nerves in post-ingestive fat preference development. While intact and left-vagotomized rats show a graded preference for increasing dietary fat, right-vagotomized rats failed to form a preference for medium-fat diets (n=15; ANOVA, Bonferroni-corrected t-tests). These experiments test the extent to which lateralized vagal CCK signaling contributes to interoceptive reward processing.

P367 **The Impact Of Iso-Caloric And Viscosity Matched High-Fat And High-Carbohydrate Drinks On Postprandial Hormonal Responses In Obese Versus Non Obese: An Experimental Study**

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Background: With rising prevalence of obesity and metabolic risks, understanding the effects of macronutrient on satiety hormones is crucial. In this experimental study, we examined whether obesity influences postprandial hormonal responses to isocaloric drinks (high-fat vs. high carbohydrate), hypothesising suppressed satiety hormone responses in obesity.
Methods: Eleven individuals with a BMI >30 kg/m² and eleven age- and gender-matched healthy-weight participants (BMI 18–25 kg/m²) completed two study visits in a randomised crossover design. At each visit, participants consumed either a

high-fat or high-carbohydrate drink following an overnight fast. Blood samples were collected at baseline (fasted state) and at multiple time points over two hours post-consumption to assess circulating levels of key satiety-related hormones, ghrelin, PYY and GLP-1, as well as glucose and insulin. **Results:** Preliminary results show that hormonal responses varied based on macronutrient composition and participant's body mass index status. High-carbohydrate drink elicited a more pronounced increase in glucose and insulin levels compared to the high-fat drink. In contrast, GLP-1 and PYY showed a greater increase following the high-fat drink. Differences in hormonal responses were observed between obese and healthy-weight participants, with obese individuals exhibiting a reduced GLP-1 response and an increased insulin response compared to their healthy-weight counterparts. **Conclusion:** Iso-caloric macronutrient composition affects postprandial GLP-1 responses differently in obesity, potentially impairing appetite control. Enhancing GLP-1 responses through diet may aid weight management and metabolic health.

P369 **Pharmacological Modulation Of The Paracannabinoid System: Protective Strategy Against Autophagy Dysregulation In Early Obesity**

Alessia Campagna[1], Christian Sepe[1], Barbara Eramo[1], Marzia Friuli[2], Elisabetta Panza[3], Ivana Bello[3], Silvana Gaetani[1], Adele Romano[1]

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Autophagy appears crucial to orchestrate fundamental aspects of cellular responses to challenging stimuli, including metabolic insults; when this process is dysregulated, it can trigger multi-organ metabolic disturbances, contributing to the development of obesity. Here we investigated autophagy alterations induced by an obesogenic diet and the potential protective effects of the pharmacological modulation of the paracannabinoids oleoylethanolamide (OEA) and palmitoylethanolamide (PEA). We developed a rat model of obesity by exposing adolescent male Wistar rats to an obesogenic diet for 7 weeks; control rats received a low-fat diet. After the induction of the phenotype, both groups were treated daily for 2 weeks either with vehicle (saline/polyethylene glycol/Tween 80) or OEA and PEA (10 mg/kg) intraperitoneally. At the end of the treatment, rats were sacrificed, liver and heart were analyzed by using histological staining, PCR array and western blot analysis. Data were statistically analyzed by using two-way ANOVA with Tukey as a post-hoc test. Histological staining reveals altered cardiac and hepatic tissue structure, increased fibrosis, and liver lipid accumulation in obese rats, partially reversed by OEA and PEA treatments. Moreover, obese animals exhibited an altered expression of autophagy-related genes. Based on these preliminary data, we observed a dysregulated protein expression of beclin-1 and p62, key markers of autophagy. Pharmacological modulation of the paracannabinoid system restored such alterations, with a more pronounced effect in PEA-treated rats. Although preliminary, our findings suggest that the modulation of the autophagic processes by paracannabinoids could offer a promising therapeutic approach for obesity-related liver and cardiac alterations.

P371 **Impact Of Gut Microbiota And Dietary Fiber On Food Intake In Obesity.**

Chaitanya K Gavini, Nadine A Eliasson, Virginie Mansuy-Aubert
University of Lausanne, Lausanne, Switzerland

Obesity resulting from hypercaloric diets disrupts gut microbiota and increases food intake. While dietary fiber supports beneficial microbes and release of satiety hormones, its direct effects on appetite remains unclear. Key questions include whether fiber influences food intake via microbial composition or short-chain fatty acids (SCFAs), the role of specific microbes, variability in fiber's effects, and its long-term metabolic impact. We hypothesized that fiber and fiber-fermenting bacteria regulate satiety and feeding behavior. To test this, mice were fed normal chow (NC), a Western diet (WD), or WD with 10% inulin (WD+I). Some WD-fed mice also received antibiotics before switching to WD+I to assess the role of gut microbiota. Mice were housed in metabolic cages to monitor food intake, meal patterns, energy expenditure, and locomotion. Body weight, composition, fasting glucose, and 16S sequencing from cecal content were also analyzed. WD-fed mice gained more weight than NC and WD+I mice due to increased fat mass. WD mice ate more frequent, larger meals, while inulin increased SCFA production, reduced meal frequency, and enhanced satiety. NC and WD+I mice had more fiber-utilizing bacteria (Bifidobacteria, Lactobacilli, Akkermansia), while WD mice had more harmful bacteria (Proteobacteria, Firmicutes) and fewer beneficial ones (Bacteroidetes). Antibiotic-treated WD mice also ate less frequently, suggesting gut microbiota influence satiety.These findings suggest dietary fiber mitigates diet-induced hyperphagia by modulating gut microbiota and SCFA production. Further research integrating microbial profiling, metabolomics, and neuroendocrine analysis is needed to clarify inulin's role in appetite regulation and obesity prevention.

P373 **A Pre-Clinical Metabolic Model Of Alzheimer&Rsquo;S Disease: Relating Metabolic Output With Hypothalamic Changes In Female App^{Nlgf} Mice.**

Rebecca Gorham[1], Solene Vardon[2], Carlota Lalanda Castro[1], Zaki A Hurst[1], John Apergis-Schoute[1]

[1]Department of Psychology, Queen Mary University of London, London, United Kingdom, [2]UniversiteClaude Bernard, Lyon, France

While cognitive decline is a hallmark of Alzheimer's Disease (AD), non-cognitive symptoms such as changes in sleep, appetite and metabolism also occur. These disruptions often precede the cognitive deficits and can predict disease progression indicating that monitoring them in susceptible individuals can act as an early diagnostic tool for detecting AD. The lateral hypothalamus (LH) is a key brain area for regulating metabolism and importantly Aβ and tau pathologies develop in the LH of those with AD. Using an AD mouse model, we are longitudinally profiling metabolism in female transgenic mice who express mutated humanised beta-amyloid precursor protein (APP^{NLGF} mice) and relating this with changes in LH orexin and MCH circuits – two peptide-expressing cell groups with well-known importance in sleep and metabolism. To do so APP^{NLGF} (n=8) and WT (n=8) mice are housed in specialized units at 6 timepoints (between 16-36 weeks) for metabolic profiling (CO_2/O_2 consumption, activity, food & water intake). Body composition is also measured using a tdNMR scanner. In separate APP^{NLGF} and WT mice (16, 28, 36 weeks: n=5/group) LH tissue is stained for orexin, MCH and APP and cell numbers quantified for determining age-related changes in APP^{NLGF} compared to control mice. Our preliminary data shows that despite similarities in body weight, APP^{NLGF} mice are higher in fat content at 16 and 21 weeks. Moreover, at 21 weeks we see a significant decrease in total locomotor activity in APP^{NLGF} mice and a trend in the same direction for wheel running. We are currently continuing to collect data at other timepoints and analysing orexin and MCH

cell populations. Doing so will shed light on the link between alterations in LH circuits and metabolism in a pre-clinical AD rodent model.

P375 **Effect Of Nutritional State And Pre-Load Meal Size On Spatial Memory For High-Energy Food In Adults Without Obesity**

Jiaxun Liu[1], Wai In Ng[1], Raghav Bhargava[1], Jialin Guo[1], Marcela Rodriguez Flores[1], Xinyi Zhang[1], Mimoza Emini[1], Wanqian Li[1], Sandra Luur[1], Zoe Barley[1], Rachelle de Vries[2], Anthony P Goldstone[1]

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Background: Food-related memory is important for eating behaviour. Pre-clinical studies have found a hippocampus-hypothalamus-midbrain circuit regulating food spatial memory activated by fasting via orexigenic hormone acyl ghrelin. In humans, virtual spatial memory was better for high-energy (HE) than low-energy foods in healthy adults (de Vries et al. 2020-22). We used this task to test the hypotheses that food intake attenuates HE food spatial memory. **Methods:** In a randomised, single-blinded study, n=17 adults without obesity (53% male, age 21-55 years, BMI 18.8-27.5 kg/m^2) attended 4 visits after an overnight fast, consuming 750mL liquid preloads of 0, 600, 900, 1200 kcal. After 125 min, they performed a computer spatial memory task to encode the location of stalls on a virtual map selling 12 HE foods and 12 objects (randomised order block design), having practised at a screening visit. 5 min later participants recalled which stall was selling each item to calculate % accuracy of stall selection and distance from recalled to correct stall. **Results:** There were no significant differences in spatial memory (accuracy or distance) for HE food vs. objects between all fed (600, 900, 1200 kcal) and fasted (0 kcal pre-load) visits (P=0.29-0.33, d -0.14 to 0.12). There were no significant correlations between spatial memory for HE food vs. objects and pre-load meal size (as absolute kcal or % estimated resting energy expenditure) (r^2=0.00-0.01, P=0.41-0.93). **Conclusion:** No evidence seen for attenuation of spatial memory for HE food by fed nutritional state or increasing preload meal size in adults without obesity. Interpretation is strengthened by within-participant multiple visit design, but limited by sample size, virtual nature, inclusion of only adults without obesity.

P377 **Examining The Probiotic, Prebiotic, And Synbiotic Potential Of Bifidobacterium Pseudolongum And Oligofructose On Energy And Glucose Homeostasis**

Andrew M Orm[1], Drew Seiser[2], Angela Ding[3], Savanna N Weninger[3], Frank A Duca[1,4]

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Obesity and Type II Diabetes (T2D) are now considered worldwide epidemics, so it is vital to explore alternative treatments. Targeting the gut microbiota could provide alternative therapies for the treatment of obesity and T2D. Several studies have shown that prebiotics and probiotics can improve energy and glucose homeostasis in obese / diabetic models. Specifically, our lab has demonstrated an acute role of the prebiotic oligofructose (OFS) and probiotic Bifidobacterium pseudolongum in reducing food intake and glucose production in obese rats, which we hypothesize could contribute to long-term improvements in body weight and glucose regulation. Therefore this study aims to explore the long-term prebiotic, probiotic, and combined synbiotic potential of OFS and B. pseudolongum, respectively, on energy and glucose homeostasis in high-fat diet-induced obese mice. C57BL/6 mice were placed on a high-fat (HF) diet for 6 weeks (wks) to induce obesity and insulin resistance. Subsequently, the mice were divided into four treatment groups, including HF control (n = 15), HF supplemented with B. pseudolongum (HF+BF) (n = 15) , HF supplemented with 10% OFS in the diet (HF+OFS) (n = 16), and HF with both OFS and B. pseudolongum (HF+OFS+BF) (n = 16) for an additional 6wks. Results indicate that while both HF+OFS and HF+OFS+BF prevented body weight gain and decreased adiposity compared to HF-fed rats, B. pseudolongum did not provide greater improvements than that of OFS alone and had no effect when administered alone. No significant changes in insulin sensitivity were observed 1wk following prebiotic, probiotic, or synbiotic treatment, but improvements in glucose tolerance were observed at 120 minutes after 1wk of synbiotic treatment and at 60, 90, and 120 minutes after 6wks using a 2way-ANOVA.

P379 **Oleoylethanolamide Ameliorates Altered Lipid And Energy Metabolism In The Skeletal Muscle Of Overweight Rats**

Christian Sepe[1], Alessia Campagna[1], Marzia Friuli[2], Barbara Eramo[1], Francesco Vari [1], Anna Maria Giudetti [3], Daniele Vergara[3], Silvana Gaetani[1], Adele Romano[1]

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Ectopic fat accumulation in sites different from adipose tissue, including skeletal muscle, is one of the main causes of obesity-related metabolic disorders. This condition of "lipid overload" leads to morphological and metabolic dysfunctions that can affect skeletal muscle function. Here we investigated the possible protective effect of oleoylethanolamide (OEA), a PPAR-alpha agonist, on skeletal muscle alterations, including fibrosis, and energy dysmetabolism in adolescent rats exposed to an obesogenic diet. For this purpose, male Wistar rats were fed a high-fat diet or a low-fat diet for 7 weeks; both groups were treated for 2 weeks either with vehicle (saline/polyethylene glycol/Tween80) or OEA (10 mg/kg, intraperitoneally). After treatment rats were sacrificed and gastrocnemius was collected and processed to assess morphological changes, lipid content, mitochondrial activity, and ATP production by using thin-layer chromatography, RT-qPCR and western blot analysis. Data were statistically analyzed by using two-way ANOVA with Tukey as a post-hoc test. Overweight rats displayed the following skeletal muscle alterations: increased fibrosis; increased triacylglycerols contents accompanied by a reduction of the expression and activity of the carnitine palmitoyltransferase-1; decreased ATP level; increased activity and the expression of the mitochondrial complexes I, II, and IV; increased mitochondrial biogenesis. All these alterations are reverted by the pharmacological treatment with OEA, which restores a physiological lipid and energy metabolism in the skeletal muscles of overweight rats. Our observations open the way for a key role of OEA in the correction of metabolic events that can act as a scaffold for the onset of muscle impairment associated with obesity.

P381 **Chrononutrition As A Shared Determinant Of Poor Sleep Onset, Increased Adiposity And Obesity In 11&Ndash;14-Year-Olds**

Emma L. Gale[1], Andrew J. Williams[2], Jo E. Cecil[1]
[1]University of St Andrews, St Andrews, United Kingdom, [2]The University of Edinburgh, Edinburgh, United Kingdom

Worldwide, 20% of adolescents are living with overweight or obesity and 68% of adolescents do not meet sleep recommendations. Diet is a determinant of weight status and caffeine consumption can impact sleep, but less is known about how chrononutrition impacts sleep and weight status. We hypothesised that late-night food consumption habits including sugar and caffeine are associated with both obesity and poor sleep. A cross-sectional study of 11–14-yr-olds in Scotland was conducted. Body mass index percentile (BMIp) and bioelectrical impedance were used to assess obesity and adiposity. Chrononutrition (late-night (1-hr before bed) sugar-sweetened beverage, caffeine consumption, time of last food consumption) was assessed via self-report. Sleep onset problems were measured using validated questionnaires and actigraphy. Regression was used to examine the association between sleep and obesity and diet behaviours, adjusting for gender, ethnicity, maternal BMI and work shift pattern, and wellbeing. Sixty-two adolescents (29M/33F, 12.2±1.13yrs) completed the study. Mean body fat % was 22.3±11.5; mean BMIp was 60.3±32.1. Mean total daily sleep was 423.2±82.4 mins (wk), 501.5±75.5 mins (wkend); 37% experienced moderate-severe insomnia. Late-night food consumption was associated with a later chronotype (AdjR^2=.830, F=34.202, p<.001), increased insomnia (AdjR^2=.753, F=18.682, p<.001), increased body fat % (AdjR^2=.749, F=21.191, p<.001) and increased BMIp (AdjR^2=.581, F=10.392, p<.001). All other diet choices/consumption habits were determinants of poor-sleep or adiposity. Chrononutrition was a shared determinant of poor sleep, obesity and increased adiposity. Late-night timing of food consumption should be a target in health-promoting interventions to improve adolescent health.

10:00 - 11:30 AM	L2
Symposium 3: What food systems can teach us about drug use and addiction	

Chair(s): Carrie Ferrario

10:00 **High-Fat Diets Attenuate Nucleus Accumbens Dopamine Release And Enhance Nicotine Reinforcement-Related Behavior In Mice**

Samuel Tetteh-Quarshie, Lauren E Young, Brandon J Henderson
Joan C Edwards School of Medicine at Marshall University, Huntington, WV, United States

Smoking and obesity are the leading causes of preventable deaths in the United States. However, studies examining the synergistic effects of obesity and smoking (including vaping) in preclinical models are sparse. Based on previous investigations, we hypothesized high-fat (obesogenic) diets alter nicotine reinforcement by attenuating dopamine (DA) release. Male and female mice (n=6 each) were exposed to vaporized nicotine after being maintained on a regular rodent diet (RD; 5% fat) or obesogenic diets (DIO; 42% or 60% fat) for 6 weeks. DA release in the nucleus accumbens core (NAcc) was assessed with fast-scan cyclic voltammetry (FSCV). We further examined whether obesity-induced neuroadaptation in the dopaminergic system modulates nicotine reinforcement-related behaviors. Here, a separate cohort of RD and DIO mice (n = 6, each condition, each sex) were trained to self-administer nicotine using an e-vape® self-administration (EVSA) assay. Obesogenic mice exhibited reduced tonic and phasic dopamine release in the NAcc and displayed a significant increase in nicotine reinforcement-related behaviors (two-WAY ANOVA). To examine circuit inputs into the VTA, we used patch-clamp electrophysiology to examine changes in intrinsic excitability in the medial prefrontal cortex (mPFC) and VTA. Here, we observed that VTA DA neurons exhibited a diet-induced decrease in excitability but layer 5 pyramidal neurons in the mPFC exhibited a diet-induced increase in excitability (*t* test). The data presented here suggest that obesogenic diet enhances nicotine reinforcement-related behaviors, and this may be modulated by disturbances in the metabolic system and neuroadaptation in neuronal physiology.

10:30 **Eating A High Fat/High Carbohydrate Or Ketogenic Diet Impacts Sensitivity Of Rats To The Effects Of Morphine**

Katherine M Serafine[1], Nina M Beltran[1], Vanessa Minervini[2]
[1]University of Texas at El Paso, El Paso, TX, United States, [2]Creighton University, Omaha, NE, United States

Eating a high fat/high carbohydrate diet has been linked to weight gain, while eating a high fat/low carbohydrate (ketogenic) diet leads to weight loss. It has been established that high fat diet consumption increases sensitivity of rats to stimulant drugs, but it is not known if sensitivity to opioids is also impacted by diet. To test the hypothesis that eating a high fat diet would increase sensitivity of rats to the effects of morphine, male rats (n=7-8/group) ate either a low fat diet, a high fat/high carbohydrate diet, or a ketogenic diet and morphine-induced antinociception was measured using the warm water tail withdrawal procedure (0.32-56 mg/kg; IP). Tolerance was induced by administering twice-daily injections of morphine for 19 days (3.2-56 mg/kg; IP). Tail withdrawal latencies were converted to a % maximum possible effect, averaged, and analyzed using mixed model ANOVAs. Several withdrawal signs were evaluated after naltrexone administration (17.8 mg/kg; SC), including weight loss and vocalization, and were averaged and analyzed using mixed model ANOVAs. There were no differences in the acute antinociceptive effects of morphine among rats eating different diets. However, tolerance was significantly greater for rats eating the high fat/high carbohydrate diet as compared to rats eating the ketogenic diet. Following naltrexone administration, withdrawal signs were more frequent, and body weight loss was more severe for rats eating the high fat/high carbohydrate diet as compared to rats eating the ketogenic diet. These results indicate that eating a high fat/high carbohydrate diet enhances morphine tolerance, while a ketogenic diet reduces the severity of withdrawal and will be discussed in the context of chronic pain treatment, as well as opioid use disorder.

11:00 **Responding For Opioids Is Reduced In Rats And Humans By Treatment With A Glucagon-Like Peptide-1 Receptor Agonist**

Patricia Sue Grigson[1], Scott Bunce[2], Timothy Brick[3], Christopher Freet[2], Erin Deneke[4], Jennifer Nyland[1], H. Harrington Cleveland[3], Sarah Ballard[1], Dean Stankoski[4], Adam Scioli[4], Joaquin Douton[1], Luke Urbanik[1], Brianna Evans[1], Christopher Brandl[1], Caleb Whitfield[1], Elise Shealy[1]
[1]Department of Neural and Behavioral Sciences Penn State College of Medicine, Hershey, PA, United States, [2]Department of Psychiatry and Behavioral Health Penn State College of Medicine, Hershey, PA, United States, [3]Department of Human Development and Family Studies Penn State University, Happy Valley, PA, United States, [4]Department of Psychiatry and Behavioral Health Penn State College of Medicine, Hershey, PA, United States, [5]Caron 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. Here we tested the safety and efficacy of glucagon-like peptide-1 receptor agonists (GLP-1RAs) for the treatment of OUD in rodent models and in humans in residential treatment. **Pre-clinical: Methods and Results.** Treatment with all GLP-1RAs tested, including exendin-4, liraglutide, semaglutide, and tirzepatide reduced heroin taking and heroin and fentanyl seeking (i.e., 'relapse') in both male and female rats and when administered acutely or chronically. **Clinical: Methods.** In a fully-randomized, double-blind, placebo-controlled study, patients in residential treatment for OUD were consented following medically assisted withdrawal, stratified by patient's choice for medication assisted treatment (MAT: buprenorphine) or No MAT, then randomized into placebo (n=10) or liraglutide (n=10) treatment 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 and Efficacy.** Daily treatment with liraglutide did not adversely affect body weight, blood glucose, or cardiorespiratory function in this population. Regarding efficacy, data gathered using ecological momentary assessment showed that liraglutide reduced craving by 40% compared to placebo (Cohen's d @.5, p=0.005), even at the lowest dose (Cohen's d @.5, p=0.005), and liraglutide treatment, compared to placebo, was associated with reduced opioid craving in the afternoon and evening ($p < 0.002$) and during times of high stress. **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.

10:00 - 11:30 AM	L1
Oral Session 5: Hot topics in ingestion and nutrition	

Chair(s): Dana Small

10:00 **Subcortical Brain Function Preferentially Aligns With An Internal Gastric Rhythm During A Food Bidding Task**

Nils B. Kroemer[1-4], Vanessa Teckentrup[2], Ignacio Rebollo[5], Manfred Hallschmid[3,4,6], Sophie J. Mueller[2]

[1]Section of Medical Psychology, Department of Psychiatry and Psychotherapy, Faculty of Medicine, University of Bonn, Bonn, Germany, [2]Department of Psychiatry and Psychotherapy, TÃƒÂƒÃ‚Â¼bingen Center for Mental Health, University of TÃƒÂƒÃ‚Â¼bingen, TÃƒÂƒÃ‚Â¼bingen, Germany, [3]German Center for Mental Health (DZPG), partner site TÃƒÂƒÃ‚Â¼bingen, TÃƒÂƒÃ‚Â¼bingen, Germany, [4]German Center for Diabetes Research (DZD), Neuherberg, Germany, [5]Department of Decision Neuroscience and Nutrition, German Institute of Human Nutrition, Potsdam, Germany, [6]Institute of Medical Psychology and Behavioural Neurobiology, University of TÃƒÂƒÃ‚Â¼bingen, TÃƒÂƒÃ‚Â¼bingen, Germany

Eating is regulated by an integration of internal and external cues. Despite mechanistic progress in the past decades, how the brain adaptively arbitrates between interoceptive versus exteroceptive processing to regulate energy metabolism remains elusive. Here, we manipulated the influence of internal and external cues using transcutaneous vagus nerve stimulation (tVNS) and a food bidding task, while measuring brain responses and gastric myoelectric activity. To quantify the integration of these cues, we evaluated their synchronization with brain signals during rest and task conditions in 27 healthy participants (20 women; see Müller et al., 2022, *Brain Stimul*). Our findings reveal that subcortical regions predominantly align with internal gastric signals, whereas cortical regions synchronize with task-related external cues. Crucially, tVNS further amplifies the synchronization with gastric signals in the nucleus accumbens during the food task (vs. sham). Correlations of brain coupling with internal versus external signals with individual differences in motivation and subjective hunger support a role in appetitive behavior. Taken together, our results highlight the vital role of internal gut signals in driving subcortical brain responses and show their modulation by vagal afferents. By bypassing the need for self-reports of interoception, our innovative approach holds great promise for future translational work to understand better how eating is regulated in an adaptive or maladaptive manner.

10:15 **Amygdala Projections To The Pons Promote Motor Programs Of Ingestion**

Danielle Lafferty, Jeremiah Isaac, Joelyz Wolcott, Amy Phan, Andrew Lutas
National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, United States

We investigated neural circuit mechanisms that allow for the overconsumption of food despite visceral satiety signals. Here we focused on the projection from the central nucleus of the amygdala (CeA) to the pons region of the hindbrain, which has been implicated in overconsumption. However, within the pons, CeA targets the parabrachial nucleus that relays visceral sensory signals as well as the nearby peritrigeminal premotor circuits that control orofacial behaviors. The contribution of these pathways to the over ingestion behavior is unknown. Using fiber photometry (n = 12) and two-photon microscopy (n = 5), we recorded the activity of CeA GABAergic axons in the pons. Axon activity levels correlated to the duration of bouts of licking for liquid food and were not modulated by physiological state or palatability, suggesting that this pathway modulates consummatory behaviors. Optogenetic activation of axons in head-fixed mice (n = 7) triggered context-specific orofacial motor behaviors, including licking and biting, as well as excessive drinking of any liquid, regardless of palatability. In freely moving, ad libitum-fed mice (n = 11), photostimulation induced biting, chewing, and swallowing which led to overconsumption of food when the stimulation occurred nearby, but not away from, food. In both head-fixed and freely moving mice, photostimulation-induced over ingestion remained sensitive to visceral signals as mice eventually stopped ingesting (n = 5). These findings support a model in which CeA axon activity in the pons enables a state of orofacial behavioral disinhibition that remains controlled by external and internal contextual cues. This disinhibition, rather than suppression of satiety signals, likely drives the overeating observed with photostimulation.

10:30 **Multilevel Encoding Of Nutrient-Based Food Valuation In The Primate Amygdala**

Fei-Yang Huang, Fabian Grabenhorst
Department of Experimental Psychology, University of Oxford, Oxford, United Kingdom

Sensory and nutrient food properties shape food valuation, guiding reinforcement learning (Huang & Grabenhorst, JNeurosci, 2023) and food choice (Huang et al., PNAS, 2021) in primates. However, it remains unclear whether single neurons in the primate reward system integrate sensory and nutrient information to encode subjective food value. Primate amygdala, a key structure in value-based decision-making, receives multisensory inputs and is well-positioned to process nutrient information during food choice, but direct neuronal evidence is lacking. Here, we examined the neuronal basis of nutrient reward valuation by recording single-unit activity from 208 amygdala neurons in two male rhesus macaques (*Macaca mulatta*) as they chose from visual cues each linked to one of the eight drinks that differ in fat, sugar, and mouthfeel (modified with tasteless thickener). Using generalized linear regression, we identified distinct neural populations encoding fat (12.02%), sugar (15.38%) and subjective value (11.06%) during visual cue presentation. Time-resolved Structural Equation Modeling (SEM) revealed that fat and sugar content contributed to the subjective value signals and that nutrient-related neuronal activity was partially mediated by oral texture properties (viscosity, oral friction). This multilevel mediation analysis uncovered a sensory-nutrient-value structure in neural reward processing, highlighting how sensory and nutrient properties contribute to food valuation within the primate amygdala. Future studies following this nutrient-reward approach could further reveal nutritional principles governing neural reward processing and adaptative food preferences in primates.

10:45 **The Addictive Potential Of Ultra-Processed Foods: Identifying Key Nutritional Predictors**

Ashley N Gearhardt[1], Zach Hutelin[2], Emmanuel Nartey[2], Monica Ahrens[2], Mary E Baugh[2], Tera L. Fazznio[3], Erica M LaFata[4], Kendrin R Sonneville[1], Alexandra G DiFeliceantonio[2]

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Research suggests that certain foods may trigger addictive processes, contributing to difficulties in controlling intake. Meta-analyses estimate that 14% of adults meet the criteria for addictive consumption of processed foods, similar to tobacco (18%) and alcohol (14%). However, food is a complex stimulus, and not all foods trigger addictive responses. We hypothesize that ultra-processed foods (i.e., industrial products typically high in refined carbohydrates/fat that are often engineered for maximum appeal and profitability) are most likely to exhibit addictive potential. A nationally representative sample (n=1664) completed the Yale Food Addiction Scale, which applies substance addiction criteria (e.g., loss of control, cravings, tolerance, withdrawal) to food consumption,and rated a random subset of 297 commonly consumed foods to examine which nutritional factors predict a food's addictive potential. The foods with the highest tertile addictive rating were overwhelmingly ultra-processed (91.8%), with none being minimally processed (0%). The dataset was split into training (80%) and test (20%) sets, ensuring stratification based on the average addictiveness rating. The training set was used for 5-fold cross-validation to identify the optimal predictive model among lasso regression, extreme gradient boosting, and random forest. Random forest analysis of 171 nutritional variables identified available carbohydrates, glycemic load, and energy density as the strongest predictors of a food's rated addictiveness based on root mean squared error. Findings suggest that energy-dense, ultra-processed foods high in refined carbohydrates may be the most addictive, guiding public health efforts to reduce compulsive consumptionof these foods, which dominate the US food market.

11:00 **Contrasting Metabolic And Neural Responses To Ultra- And Minimally Processed Foods.**

Zach Hutelin[1,2], Monica Ahrens[3], Mary Elizabeth Baugh[2], Bert Herald[2], Alexandra L. Hanlon[3], Alexandra G. DiFeliceantonio[2,4]

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Dietary patterns have shifted toward increased consumption of ultra-processed foods (UPF), which has been linked to higher rates of preventable mortality. Although orosensory properties likely influence intake, one understudied factor is differences in post-oral signals. Here, we recruited 38 healthy weight adults aged 18-45 to examine the role of food processing on brain and metabolism. First, we performed an auction paradigm concomitant with functional magnetic resonance imaging (fMRI), where participants bid on 14 UPF and 14 minimally processed foods (MPF). Although willingness-to-pay (WTP) was not different for MPFvsUPF, BOLD response associated with WTP was greater for MPFvsUPF in the fusiform gyrus, visual cortex, thalamus, and striatum (all $T>4$, $p<0.01$). On separate days we performed two 4-hour whole room indirect calorimetry metabolic measurements with simultaneous blood draws, during which participants consumed either a UPF or MPF meal (300 kcal). Meals were matched within ~1% of energy, weight, macronutrients, fiber, and glycemic load and index. The UPF meal evoked a higher metabolic rate ($p<0.05$), while the MPF meal respiratory quotient (RQ) was higher ($p<0.05$), and there was a time by condition interaction for blood glucose ($p<0.01$). Next, we examined the association between post-oral signals and brain response. Difference in peak RQ was significantly associated with activation in the amygdala and ventral striatum (all $T>5$, $p<0.03$). The difference in blood glucose response at minute 20 was associated with activity in dorsomedial prefrontal and anterior cingulate cortex (all $T>5$, $p<0.001$). These data demonstrate that even matched for nutritional profile, MPF and UPF produce different post-oral signals, and those signals influence brain response to food cues.

11:15 **Ultraprocessed Food Consumption Affects Structural Integrity Of Feeding-Related Brain Regions Independent Of And Via Adiposity**

Arsene Kanyamibwa[1], Filip Morys[2], Daniel Fangstrom[1], Max Tweedale[2], Alexandre Pastor-Bernier[2], Houman Azizi[2], Lang Liu[2], Annette Horstmann[1], Alain Dagher[2]

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Ultra-processed foods (UPFs) are industrial formulations with multiple ingredients that undergo extensive processing and constitute a significant portion of modern diets. UPF consumption can lead to adverse outcomes such as brain pathology (i.e., dementia) through increases in adiposity or other adiposity-independent pathways. Our study explored mechanisms by which higher UPF consumption is linked to structural brain changes, potentially contributing to a vicious cycle between diet and disease. To investigate these effects, we analyzed data from 33,654 participants (mean age at imaging assessment = 64.5 years, mean BMI = 26.09kg/m2, 17,234 women) in the UK Biobank. Using general linear model (GLM) analyses, we examined the relationship between self-reported UPF consumption and brain structure, followed by mediation analyses to explore potential pathways involving anthropometric and cardiometabolic variables. Our results indicate that higher UPF consumption is associated with changes in cellularity in the right nucleus accumbens (NAcc) and hypothalamus, as well as alterations in water content in the right NAcc. Additionally, we found that UPF consumption correlates with multiple anthropometric, metabolic, and dietary measures. These results could reflect neuroinflammation as part of a neurodegenerative process since our mediation analyses revealed that the relationship between UPF consumption and NAcc cellularity was influenced by inflammatory markers, while BMI mediated the association between UPF consumption and hypothalamic cellularity. Our findings indicate that UPF consumption is associated with poor metabolic health and neuroinflammation through adiposity and independent of it.

11:30 - 1:00 PM	On Own
Lunch	

11:45 - 12:45 PM	L2
Meet the Scientist, organized by the New Investigator Advisory Committee	

This event will offer new investigators the opportunity to network with established scientists and industry professionals.

Lunch provided afterward for 65 registrants.

We ask new investigators to sign up for this event using the following link: https://linkyme.com/?NIACMTS.

1:00 - 2:00 PM	L1
MARS Lecture 3 - Daniel Nettle, Institut Jean Nicod	

Chair(s): Jeff Brunstrom

1:00 **Food Insecurity: What Is It, Who Experiences It, And Why Is It So Strongly Associated With Health Outcomes?**
Daniel Nettle
Institut Jean Nicod, Paris, France

Food insecurity—defined as limited or uncertain access to adequate and nutritious food—is surprisingly prevalent in affluent countries, and quite strongly associated with obesity, poor health, and premature mortality. What do these associations actually mean in causal terms? Someone is classified as experiencing food insecurity if they answer 'yes' to one or more items on a food-insecurity questionnaire. But the questions mention quite a lot of different things, notably *being worried*, *not having enough money*, and *being hungry or not having enough to eat*. Thus, food insecurity could mostly be picking up: psychiatric morbidity (anxiety); low income; inadequate nutrition; or some combination of all of these. We thus need to ask: under what circumstances do people answer 'yes' to food insecurity questions, and what do we know about the ingestive behaviour of people who do so? On the former question, food insecurity is a fairly direct consequence of a low income relative to household requirements. It is one of a series of deprivations that occur progressively as income diminishes and people become unable to secure increasingly basic needs. Being materially deprived in this way causes people to feel more anxious and depressed. On the latter question, the main differences seem to reside not in the overall amount of hunger or intake, or in dietary composition, but rather in the temporal variability of ingestion, especially from day to day. I will discuss implications for the epidemiological literature on food insecurity and health.

2:00 - 3:00 PM	North & South Mezzanines
Poster Session 5, Exhibits & Coffee Break	

Poster numbers 300-346 are located in the South Mezzanine. Poster numbers 347-384 are located in the North Mezzanine.

P302 **Regulation Of B-Arrestin Signaling In The Dorsal Vagal Complex Parses Satiety And Glycemic Control From Nausea/Emesis Behaviors**

Caitlin Baumer Harrison[1], Danya Aldaghma[2], Allison Pataro[3], Allaha Mohiby[2], Brandon Alonso[1], Alex White[4], Yue-Wei Qian[4], Francis S Willard[4], Minrong Ai[4], Kyle W Sloop[4], Tito Borner[3], Bart C De Jonghe[2], Matthew R Hayes[1]
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Glucagon-like peptide-1 receptor (GLP-1R) agonists suppress food intake, body weight, and blood glucose but are associated with nausea/emesis in many patients. Thus, novel GLP-1R agonists are needed to minimize these side effects while preserving beneficial metabolic outcomes. Exendin-4-Phe1 (Ex-Phe1), a modified GLP-1R agonist, is reported to induce biased agonism of the GLP-1R. Ex-Phe1 favors cAMP signaling with reduced β-arrestin (βarr) recruitment in cell lines from multiple species. Using mice, rats, and musk shrews we showed reduction in blood glucose was similar following systemic administration of either Ex-4 or Ex-Phe1 in all three species. Ex-Phe1 significantly reduced emetic episodes in musk shrews and showed no kaolin intake (nausea proxy) in rats compared to Ex-4. Ex-Phe1 had varying effects on food intake and body weight: it more robustly suppressed food intake and body weight in mice, had attenuated effects in musk shrews, and had no effect in rats. In mice and shrews, Ex-4 and Ex-Phe1 induced similar c-Fos in the area postrema (AP) and nucleus tractus solitarius (NTS). In rats, Ex-Phe1 induced similar c-Fos in the NTS but reduced expression in the AP compared to Ex-4. These results highlight the importance of understanding the requirement of barr in eliciting the anorectic and illness-like behaviors from GLP-1R agonists. Ongoing studies using a βarr antagonist in shrews and rats aim to address this. Collectively, these results indicate that biased actions of Ex-Phe1 is effective for glycemic control in mice, rats, and shrews, but 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 biased agonism of the GLP-1R for the future treatment of diabetes.

P304 **Development And Validation Of A Food Frequency Questionnaire To Assess Fermented Food Consumption In Adults**

Aimone Ferri[1,2], Elizabeth Schneider[1], Alice J Lucey[3], Paul D Cotter[1,4], Ramya Balasubramanian[1,2,4], Ã ƒÂ·ine Hennessy[3,5], Gerard Clarke[1,6], John F Cryan[1,2]

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Background: Fermented foods are gaining popularity in Western cultures, partly due to their purported health benefits via the microbiota-gut-brain axis. Consequently, there are increasing calls for fermented foods to be included in national dietary guidelines, but there are no existing validated tools to comprehensively assess fermented food intake. This study aimed to develop and validate a fermented food intake questionnaire (FFIQ) to assess habitual intake in adults aged 18–60 years from English first-language countries: United States, Canada, United Kingdom, Ireland, Australia and New Zealand. **Methods:** A 33-item self-administered FFIQ, informed by available international food consumption data from adults, was developed and then validated in an online sample of 167 (51% females, M_{age} = 38 ± 11) adults recruited through *Prolific* (Prolific.com). Six 24-hour automated dietary recalls (intake24.com) were used as the reference method. Correlation and Bland–Altman plots were used to assess agreement and bias between the FFIQ and the 24-hour dietary recalls. **Results**: The most frequently consumed fermented foods were cheeses, yoghurt and fermented meats. Median (IQR) intake of total fermented food was 85.4 (42.3 - 143.0) g/d for the FFIQ and 54.9 (20.8 - 112.1) g/d for the average of the 24-hour recalls, respectively. Fermented food intake as measured by the FFIQ and the 24-hour recalls showed good agreement for total fermented food intake ($r = 0.56$, $p < 0.001$), as well as for most fermented food categories (cheeses, dairy, beverages, meats and vegetables), and individual fermented foods. The Bland-Altman plots showed good agreement for total fermented food intake between the FFIQ and the 24hr recalls. The FFIQ correctly classified 93.4% of participants in the same or adjacent tertile of total fermented food intake. Moreover, the FFIQ captured episodically consumed fermented foods (e.g., kombucha, kefir, sauerkraut) that are not assessed by existing food frequency questionnaires. Test-retest reliability of the FFIQ was moderate to excellent (ICC range: 0.52-0.95) for 27 out of 33 food items. **Conclusions**: The FFIQ provides a good estimate of fermented food consumption among adults from English-first language countries. This will be a useful, freely available resource for the field with potential applications in clinical and epidemiological research aimed at exploring the link between fermented food consumption and health outcomes.

P306 **Olfactory Detection Of Sugars**

Elizabeth Hamel[1], Ellie Williams[2], Alan Spector[2], Adam Dewan[2]

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Prior studies suggest that mice can detect carbohydrates through the olfactory system. However, there has never been a rigorous psychophysical examination of the olfactory sensitivity of mice to sugars. Here, we tested the ability of head-fixed wildtype (WT, n=6-8) and knockout mice lacking a T1R3 subunit of the T1R2/3 “sweet” taste receptor (R3KO, n=6) to detect the volatiles emanating from reagent grade sugars, using an operantly conditioned Go/No-Go task combined with a high-precision olfactometer. WT mice displayed high sensitivity to the odor of these stimuli, with log10 thresholds (EC50) of -1.24+/-0.06 (~0.05M) glucose, -1.173+/-0.08 (~0.06M) fructose, and -0.57+/-0.27 (~0.27M) sucrose. R3KO mice were able to detect glucose with a similar sensitivity to WT animals, with a log10 threshold of -1.42+/-0.09 (~0.04M). Given their low volatility, the olfactory component of these stimuli likely arises from volatile contaminants associated with either the production or storage of these sugars. In a gustometer, designed to minimize the detection of orthonasal odors, R3KO mice exhibit a relative incompetence in sugar taste detection tasks, while WT mice have a reported taste threshold of ~0.17M glucose, ~0.07M fructose, and ~0.03M sucrose. In summary, these results indicate that R3KO mice can detect odor cues present in sugar solutions with similar sensitivities to WT mice. Comparing the detection limits of sugars across sensory modalities, mice appear to be more sensitive to the taste of sucrose, and more sensitive to the smell of fructose and glucose. The notable sensitivity of mice to the odors of sugar solutions, regardless of their chemical source, highlights the importance of considering the contribution of the olfactory system to taste-guided behavior.

P308 **Structure&Ndash; And Control&Ndash; Based Food Parenting As A Predictor For Child Relative Reinforcement Value Of Food.**

Hannah E. Kolpack[1], Lori A. Hatzinger[1, 2], Jennifer L. Temple[1], Katherine N. Balantekin[1]

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Food parenting and the relative reinforcement value of food (RRV) are independently related to child development of overweight and obesity (OW/OB). There is little published work on relationships between these two obesogenic factors, therefore our aim is to assess the relationships between structure- and control-based food parenting and child RRV. Data presented are from the first visit of a longitudinal study examining relationships between parent and child eating behaviors, food parenting, and weight status. 126 parent-child dyads (8-11; 51% girls) completed visit one. Both parent and child had their heights and weights measured, the parent completed the Structure and Control in Parent Feeding (SCPF) questionnaire, and child RRV of a high energy dense (HED) food was assessed. Linear regression was used to examine if the SCPF superfactors (control and structure) and subscales (restriction, pressure to eat, consistent feeding routine, and limit exposure) predicted child RRV. For the total sample and for child participants with healthy weight, structure- and control-based food parenting did not predict child RRV (*ps* > .188). For child participants with OW/OB, parent level of consistent feeding routine negatively predicted child RRV ($p = .026$), but there was no relationship with the other subscales and the superfactors (*ps* > .101). This relationship indicates that for children with OW/OB, parent use of consistent feeding routines can be protective against higher RRV. Overall, these data suggest that there is little relationship between structure- and control-based food parenting and child RRV, but other measures of food parenting could be explored.

P310 **Molecular And Functional Heterogeneity Of Camkii Alpha Neurons In The Lateral Hypothalamus: Encoding Appetitive Motivation Over Food Consumption**

Young Hee Lee, SheeJune Park, HanGyeol Bae, DongHoon Lee, MinSeo Koo, Hyung Jin Choi
Seoul National University, Seoul, South Korea

The lateral hypothalamus (LH) contains diverse neuronal populations with distinct roles in feeding regulation. Calcium/Calmodulin-Dependent Protein Kinase II alpha (CaMKII alpha) has long been known as a marker for excitatory neurons that suppress feeding behaviors in LH. Based on our interpretation of scRNA sequencing and MERFISH data, however, LH CaMKII alpha neurons exhibit molecular heterogeneity, encompassing Vglut2-positive, Vgat-positive, and non-canonical neuronal subtypes. Moreover, in vivo fiber photometry and miniature endoscope imaging reveal that these neurons are activated during appetitive behaviors, such as food-seeking and operant tasks, but are suppressed upon food contact. Optogenetic activation of LH CaMKII alpha neurons does not increase food intake, while their inhibition during food-predicting cue presentation reduces cue-potentiated feeding. Our study highlights the heterogeneity and functional specificity of LH CaMKII alpha neurons, which primarily encode appetitive motivation rather than directly promoting food consumption.

P312 **Including Fruit Juice As One Of The 5-A-Day: The Impact On Adherence To Guidelines And Markers Of Health**

Courtney Neal, Kirsten Brandt, Georg Lietz, Anthony W. Watson, Oliver M. Shannon
Newcastle University, Newcastle upon Tyne, United Kingdom

Despite well-established links between fruit and vegetable (FV) intake and myriad health outcomes, most individuals do not meet current recommendations to consume 5 portions/day. Therefore, feasible and acceptable strategies to increase FV intake are needed, especially for low consumers. Consumption of fruit juice (FJ) could help overcome common barriers to FV intake, as it is palatable, relatively inexpensive and readily available. However, the contribution of FJ to daily FV targets is contentious due to concerns about its sugar content and lower fibre levels (compared with whole fruit). This open-label, parallel arm randomised controlled trial explored the acceptability and impact of 5-a-day advice, with/without the inclusion of FJ, on FV intake, mood, gut symptoms and markers of metabolic health. Forty-two participants aged 18-65 who consumed ≤2 portions of FV/day were randomised to one of three arms for four weeks: (1) Habitual diet control, (2) Whole FV, or (3) Whole FV plus FJ. All received weekly vouchers, and the two intervention arms received behaviour change support via a co-designed educational booklet. Pre- and post-intervention, participants reported four 24-hour dietary recalls, completed mood questionnaires (PHQ-9 and GAD-7), and provided venous blood samples to allow quantification of circulating ascorbic acid and carotenoids (as objective markers of FV intake) and metabolic markers of health. Additionally, at the endpoint, participants self-reported changes in gut symptoms and completed an acceptability questionnaire. Our findings will provide important information on the contribution of FJ to 5-a-day recommendations and have the potential to inform future interventions, public health guidelines and policy. Clinical Trials Registration: NCT06628401.

P314 **Household Food Insecurity And Parenting Practices Related To Independent Eating Occasions**

Rickelle Richards[1], Grace Shearrer[2], Amanda Ziegler[3], Lillie Monroe-Lord[4], Alex Anderson[5], Jinan Banna[6], Carolyn Gunther[7], Blake Jones[1], Karina Lora[8], Glade Topham[9], Siew Sun Wong[10]
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Rationale/premise. Parenting practices that make healthy foods available for adolescents to eat when parents are not around (defined as independent eating occasions or iEOs) has been associated with increased fruit and vegetable intake among adolescents. Parenting practices used to encourage adolescents' consumption of healthy foods during iEOs may differ by household food security, given economic constraints may alter the home food environment. Hypothesis. Households with food insecurity (vs. food security) will have lower mean scores on the parenting practices of availability, expectations, and modeling, and higher mean scores on parenting practices of monitoring and indulgence as it relates to iEOs. Procedures. Parent-adolescent (11-14 y) dyads (n = 622) completed surveys related to iEOs-focused parenting practices. Parents responded to the United States Department of Agriculture 6-item food security module and demographics. Descriptive statistics and independent t-tests were used. Results. Fifty-two percent of households were food insecure. Mean scores for parent- and adolescent- reported indulgent food parenting practices were higher among households with food insecurity vs. food security ($p<0.001$). The mean score for adolescent-reported healthy food availability was lower among households with food insecurity vs. food security ($p<0.001$). Conclusions/relevance. In households with food insecurity, parent-adolescent dyads reported higher indulgent parenting practices, including allowing adolescents to consume or prepare unhealthy foods during iEOs. Only adolescents reported less healthy foods were available for iEOs, suggesting differing perspectives than parents. Strategies are needed to support healthy food parenting strategies among households with food insecurity.

P316 **Characterisation Of Microstructure Of Ingestive Behaviour In The Trained Status Of University Rowers**

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The effect of metabolism on ingestive behavior is unclear. Humans who suffer from obesity show altered microstructural ingestive patterns. Bariatric surgery can not only improve weight management but also modify this behavior. If training status in humans also affects the microstructure of ingestive behavior is yet to be investigated. We hypothesize that humans with trained status (TS) will show significant differences in microstructure of ingestive behavior in comparison to individuals with untrained status (US). University students (16 TS from a rowing program, and 7 US; recruitment ongoing) were invited to 3 study visits. At each visit, the individuals were provided with one of 3 test stimuli to consume ad libitum with a drinkometer device for the recording of microstructural parameters. The stimuli were a high-carbohydrate (HC), a high-sugar (HS) and a high-fat (HF) liquid meal, randomly assigned. Differences between the two groups were tested with ANCOVA and post-hoc comparisons. We observed that TS presented a different microstructural architecture. Burst-independent parameters showed stimulus-dependent changes from HF for suck energy intake (+14 kcal, $p<0.01$), suck duration (+0.7 s, $p<0.01$) and suck rate (+2.3 kcal/s, $p<0.05$). Burst-dependent changes were mostly stimulus-independent. Specifically, the number of bursts decreased (-18, $p<0.001$) but the energy intake per burst (+190 kcal, $p<0.01$) and burst duration (+25 s, $p<0.05$) increased with a larger number of sucks per burst (+12, $p<0.05$). For the first time, this study observed microstructural differences in ingestive behavior due to TS. A possible role of gut hormones for this difference will be investigated by analyzing blood samples that were taken from all study participants before and after the meal tests.

P318 **Do Sweet-Liking Phenotypes Differ In Habitual Smoking, Alcohol And Caffeine Intake?**

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Previous research suggests that a higher sweet taste preference may predict increased substance abuse. However, to date, studies examining this topic have either treated sweet liking as a continuous variable or used preference or choice tasks rather than liking measurements to define sweet liking groups. Our lab has repeatedly shown three distinct subgroups based on their profiles of liking for sucrose: extreme sweet-likers, moderate sweet-likers and sweet dislikers. Here, we explored how these different sweet-liking phenotypes differed in habitual use of the three most widely used legal substances: alcohol, caffeine and nicotine. Participants aged 18-45 (mean age 20) attended a single laboratory session, comprising 211 women and 55 men (mean BMI 22.9; range 16.1–36.5). To classify sweet liking, they rated liking and intensity of two samples of 1.0M sucrose and two water controls: extreme sweet-likers (n = 83), moderate sweet-likers (n = 110) or sweet-dislikers (n = 50): 28 behaved erratically and were omitted from further analysis. Linear models of alcohol use measured using the Alcohol Use Questionnaire found no significant difference in alcohol units consumed per week or binge drinking between phenotypes. Caffeine intake, estimated from the frequency of consumption of caffeinated products, also found no significant differences. Finally, whether participants smoked, used e-cigarettes (vaped), or neither was compared between phenotypes. The overall distribution differed between phenotypes (Chi-square (6) = 24.01, p = .005). Here, 65% of extreme sweet-likers neither smoked nor vaped, compared to 26% of sweet-dislikers. These data do not confirm sweet-liking as a risk-factor for alcohol use but instead suggest a strong liking for sweetness as a major disincentive to smoke.

P320 **Acute Erythritol And Xylitol Intake Does Not Affect Markers Of Platelet And Endothelial Activation**

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Metabolic profiling studies link elevated endogenous erythritol and xylitol to conditions such as cardiovascular disease. A pilot trial suggests that these sweeteners may acutely enhance platelet aggregation within 30min, though it varies naturally with diet and activity.We conducted a randomized, double-blind, placebo-controlled crossover trial to assess the acute effects of oral administration of erythritol, xylitol, and water on platelet/endothelial activation and plasma erythritol/xylitol concentrations. Eleven healthy, lean participants attended 3 different test sessions, receiving either 50g erythritol or 33.5g xylitol dissolved in 300mL water, or 300mL water.Platelet aggregation was measured *ex vivo* before and 60min post-administration.Blood samples for measurement of platelet (p-selectin) and endothelial (sVCAM-1) activation *in vivo* were collected before and up to 180min, for erythritol/xylitol concentrations up to 48h post-administration.The statistical analyses included linear mixed models and correlation analysis. Maximum platelet aggregation shows notable inter-individual and inter-visit variability. Mean±SD values fasting *vs*. 60min post-administration were: erythritol 62.28±29.27%*vs*.59.02±28.82%,xylitol 78.17±22.20%*vs*.72.93±26.20%,water 58.07±28.29%*vs*.57.45±29.69%.P-selectin and sVCAM-1 concentrations showed no significant differences between treatments and no correlation with changes in platelet aggregation.Erythritol and xylitol concentrations increased after administration of the respective sweetener but returned to baseline within 48h (erythritol) and 24h (xylitol). Our findings suggest that acute erythritol or xylitol administration does not directly affect markers of platelet and endothelial activation.

P322 **Multi-Modal Phenotyping Of Eating Behaviour Including Food Hedonics And Cue Reactivity In Adults With Obesity And Binge Eating Symptoms**

Isabelle Franco[1], Navpreet Chhina[1], Moaz Al Lababidi[1], Ghadah Aldubaikhi[1], Alisa Musatova[1], Aruchuna Ruban[2], Christina G Prechtl[3], Graham Finlayson[4], Julian P Teare[2], Anthony P Goldstone[1]
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Background: Binge eating symptoms (BES) are characterised by recurrent episodes of eating large amounts of energy-dense, palatable foods with loss of control, without compensatory behaviours. The pathophysiology of BES remains unclear, particularly if there is heightened high-energy (HE) food hedonics, cue reactivity or motivation. **Methods:** 44 adults with obesity ± type 2 diabetes mellitus (75.0%) were classified with (≥1 binge episode/month, n=24) or without (n=20) BES (BMI/sex-matched). After an overnight fast, outcomes were: (i) liking/wanting for savoury/sweet (Sav/Sw), low/high-fat (LF/HF) foods, (ii) HE and low-energy (LE) food cue reactivity using picture evaluation fMRI task (n=41), (iii) taste pleasantness/intake (kcal as % estimated resting energy expenditure) during *ad libitum* lunch with Sav/Sw, LF/HF dishes, (iv) motivation for sweets in progressive ratio task (PRT) 2 hours post-prandially, (vi) appetite/hunger ratings. **Results:** BES group had greater explicit liking/wanting and implicit wanting for HF vs. LF foods than nonBES group (P<0.001-0.008, still significant with BMI or plasma glucose as covariates), but not for Sw vs. Sav foods (P=0.40-0.88). There was no greater BOLD signal to HE food in BES than nonBES group in whole brain or ROI (reward system) analyses. There were no significant group differences in appetite/hunger ratings, taste pleasantness/intake (total, LF/HF, Sav/Sw), nor breakpoint in PRT. **Conclusions:** BES was associated with greater liking/wanting for HF foods but not sweet foods, though there was no enhanced HE food cue reactivity (possibly due to mixture of HF/sweet foods in fMRI block design), or *ad libitum* HF food intake (possibly due to limited selection). Increased hedonics to HF foods, may be an endophenotype promoting binge eating.

P324 **Income Levels As A Moderator Of Multi-Level Supermarket Discounts On Fruit, Vegetable (Fv), And Non-Caloric Beverage (Ncb) Intake And Body Weight: A Randomized Controlled Trial.**

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Rationale: FV prices are relatively high vs other foods. Interventions to incentivize FV purchases and intake may have variable effects across income groups. **Hypothesis**: Discounting FV and NCB should lead to increased FV and NCB intake and lower body wt, with larger effects for low income participants. **Methods**: Adult supermarket primary shoppers (n=312), 18-70, BMI ≥ 25, were recruited from NYC Foodtown markets, 2018-21. There was an 8-wk baseline, a 32-wk intervention with 30%, 15%, or 0% (control) randomized discounts on FV and NCB, and a 16-wk follow up without discounts. Primary outcomes were: FV and NCB (g) and body wt (kg). Dietary intake was assessed via unannounced 24-h recalls on 2 wkdays and 1 wkend day, 1 mo prior to body wt measures at wk 8, 24, 40, and 56. Annual household income and size was obtained by questionnaire at wk 8. Income was categorized as % of federal poverty level (FPL) into low (<130% FPL), middle (130-350% FPL), or high (>350% FPL). The final analysis had 33 in the 30% group, 38 in the 15% group, and 36 in the 0% group. Linear mixed models were used to detect interactions between group, time, and income. **Results**: Main effects across income groups. The 15% discount group (vs 0%) had greater fruit intake from baseline to end of followup ($p<0.001$). The 30% group (vs 0%) increased vegetable intake from baseline to mid-intervention ($p=0.028$). The 30% group (vs 0%) increased diet soda intake from baseline to mid-intervention ($p=0.001$), to end of intervention ($p=0.046$), and follow-up ($p=0.012$). The 30% group (vs 0%) lost more weight from baseline to mid-intervention ($p=0.009$). Discount effects by income level. *Fruit*: Low income earners (vs middle and high income) in the 15% group (vs 0%) increased intake from baseline to end of intervention (p's<0.02). *Vegetables*: No significant interactions were observed. *Diet soda*: High income earners (vs low and middle) in the 30% group (vs 0%) increased intake from baseline to mid intervention (p's<0.05). *Body wt*: Low income earners (vs middle and high) in the 15% group (vs 0% and 30%) lost more weight between the baseline and follow up (p's<0.04). Conclusion: Supermarket discounts increased FV and diet soda intake, and induced wt loss, with greater fruit intake and wt loss among low-income individuals, and greater diet soda intake among high-income participants.

P326 **The Association Between Prenatal Maternal Distress And Offspring Negative Affect Is Mediated By Prenatal Vitamin C Supplementation**

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Negative affect (NA) reflects infant neurobehavioral health and high NA is an early risk factor for psychopathology. Prenatal maternal depression, anxiety, and stress have been linked to higher infant NA, suggesting developmental programming effects. Given its anti-inflammatory and stress-regulating properties, we hypothesized that prenatal vitamin c intake may mediate the maternal distress to infant NA pathway. During the 2nd and 3rd trimesters, 302 pregnant participants completed 6, nonconsecutive 24-hour dietary recalls (3/trimester), and reported vitamin c supplementation. Participants also completed assessments of depression (Center for Epidemiological Studies-Depression [CES-D], Edinburgh Postnatal Depression Scale [EPDS]), anxiety (State-Trait Anxiety Inventory [STAI], Beck Anxiety Inventory [BAI]), and stress (Perceived Stress Scale [PSS]). At six months postpartum, caregivers reported infant NA via the Infant Behavior Questionnaire-Revised. Confirmatory factor analysis supported a latent maternal distress variable, using 3rd trimester CES-D, EPDS, STAI, BAI, and PSS as indicators. Higher 3rd trimester maternal distress was correlated with higher infant NA at 6 months ($r=0.21$, $p<.001$). Adjusting for covariates, a structural equation model showed that 3rd trimester vitamin c supplementation, but not dietary intake, mediated this association ($\beta=.02$, p

P328 **Enhanced Insulin-Induced Brain Response In Dorsal Striatum Functional Connectivity Is Associated With Weight Loss In Humans**

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Insulin action in the brain affects functional connectivity (FC) of mesolimbic circuitry, with subsequent effects on behavior and peripheral metabolism. Impaired insulin action in the brain negatively impacts long-term weight maintenance. In the current study, we investigated the effects of brain insulin on FC in persons who were able to lose body weight compared to a BMI-matched control group. Participants with overweight or obesity were divided into groups based on their previous voluntary weight loss. The weight loss group lost at least 5% body weight (n=17, age=57.9±7.55, BMI=29.1±4.29), and the weight-stable group maintained their body weight over the last 6 months (n=20, age=63.6±6.48, BMI=28.3±5.13). Resting-state fMRI was assessed before and 30 min after intranasal insulin (INI) delivery to the brain to evaluate FC of the mesolimbic circuitry. The results were corrected for multiple comparisons (p-FWE<0.05, whole-brain corrected). Food cravings were assessed via questionnaire (FCQ). Age, sex and BMI were used as covariates. An interaction between group and insulin spray was found for dorsal striatum FC with the right superior and medial frontal cortex. In response to INI, the weight-stable group showed decreased FC ($p=0.02$), while the weight-loss group increased FC ($p=0.004$). Food craving rating was significantly associated with the insulin-induced dorsal striatum FC (interaction FCQ X group: $p=0.049$).

Individuals with overweight or obesity who voluntarily lost body weight show higher insulin responsiveness in the dorsal striatum to prefrontal cortex functional connectivity than BMI-matched controls who did not lose weight. Hence, weight loss is potentially associated with higher insulin sensitivity in brain regions linking reward to cognitive processes.

P330 **Dopamine D2R-Neurons In The Paraventricular Thalamus Regulate Feeding, Energy Balance And Body Homeostasis.**

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The paraventricular thalamus (PVT) has recently emerged as a critical hub involved in the regulation of cognitive processes but also in the integration of homeostatic and visceral signals, thus controlling adaptive and food-seeking behavioural responses. However, despite growing evidence, the neural mechanisms by which the PVT neurocircuitry gates feeding, energy balance and nutrients partitioning remain largely unknown. Here, we show that a specific population of PVT-neurons, notably those expressing the dopamine D2 receptors, promptly and bidirectionally (activation/inhibition) gate feeding behaviours, body homeostasis and energy balance, thereby contributing to the control of energy-related (mal)adaptive responses in both physiological and obesogenic contexts. In addition, by combining complementary cutting-edge strategies (virally mediated activation/inhibition, *ex vivo* electrophysiology and *in vivo* fiber photometry for Ca^{2+} and dopamine dynamics) to functional metabolic readouts, we describe PVT D2R-neurons as gatekeepers of hunger and satiety in lean and obese animals. Our results may lead to a new understanding of unconventional brain circuits involved in food-related disorders and may provide new therapeutic solutions to counterbalance obesity-associated dysfunctions.

P332 **Lean Mass Influences The Impact Of Energy Intake On Insular Cortex Flavor Responses**

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In humans, the primary gustatory region is located in the mid dorsal insular cortex, although additional insular regions overlying the opercular cortex also respond to flavors (Small 2012). In this preliminary study, we seek to identify areas of the insula/operculum that respond to a sweet flavored beverage and to determine whether these responses are influenced by changes in internal state, perception and body composition. Fourteen healthy-weight participants underwent a 7 Tesla fMRI study. Small boluses of flavored solution and a control flavorless solution were delivered to subjects in the scanner before and after they consumed 100kCal of the same flavored beverage. Functional data were preprocessed using FSL, spatially normalized with ANTs, and statistically analyzed with SPM 12. To identify regions that responded irrespective of the internal state, we employed a conjunction analysis on the main effects of flavor vs tasteless during pre and post drink. This analysis revealed an activated region in the mid insula - extending from dorsal to ventral portions. Contrast analyses were used to identify regions with differential responses to flavour as a function of state, but none were statistically significant. However, lean mass was negatively associated with the impact of the beverage consumption on insular response such that individuals with higher lean mass had smaller changes over time ($p=0.001$, FDR corrected). No effects of perception or fat mass were observed in this healthy-weight sample. These preliminary results demonstrate an association between lean mass and the effect of energy consumption on insular responses to flavors, possibly reflecting lower energy requirements related to higher lean mass.

P334 **Opposite Effects Of Social Stress On Prefrontal Cortical Outputs To The Amygdala And Accumbens - Possible Mechanisms For Binge-Eating.**

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Background: Stress alters decision-making, promoting impulsive behavior and excessive consumption of palatable foods. The prefrontal cortex (PFC) regulates these behaviors by integrating dopaminergic signaling to control reward processing. Stress-induced dopamine release in the PFC can reshape neuronal excitability, potentially driving maladaptive eating. Dopamine D1 receptor-expressing (D1) neurons in the PFC that project to the basolateral amygdala (BLA) or the nucleus accumbens (NAc), reveal to be a non-overlapping population, potentially responding differently to dopamine release by stress in PFC. Hypotheses: (1a) Social stress induces pathway-specific plasticity in PFC(D1) neurons, enhancing excitability of PFC-BLA projections while suppressing PFC-NAc activity. (1b) Enhancing the activity of the PFC-BLA pathway increases impulsive eating while increasing the PFC-NAc pathway reduces impulsive feeding. Methods & Results 1. Histology: Viral tracing in D1-Cre mice shows PFC(D1) neurons projecting to the BLA and NAc form non-overlapping populations, indicating pathway-specific functions. 2. Electrophysiology: Social stress enhances excitability of PFC(D1)-BLA neurons but reduces excitability of PFC(D1)-NAc neurons, suggesting bidirectional modulation of PFC output. Stimulating post-stress PFC(D1) terminals in BLA or NAc does not alter synaptic transmission, indicating stress affects somatic, rather than synaptic, plasticity. 3. Chemogenetics: Enhancing PFC-BLA excitability increases fat intake & inhibition reduces it. PFC-NAc modulation does not affect feeding Conclusions: Stress induces somatic plasticity of PFC(D1) neurons, selectively enhancing PFC-BLA excitability. This upregulation drive stress-induced impulsive eating, while PFC-NAc projections remain unaffected.

P336 **Unraveling The Dopaminergic Populations Underlying Hyperactivity And Anxiety In Activity-Based Anorexia**

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Anorexia nervosa (AN) is a metabo-psychiatric disorder with one of the highest mortality rates among psychiatric disorders. Patients exhibit a range of symptoms, including fear of weight gain, anxiety, hyperactivity, and low BMI. Despite its severity, the underlying pathophysiology remains poorly understood. A key area of interest is the dopaminergic system, given that AN patients display reward-processing deficits. While rodent studies using the activity-based anorexia (ABA) model reveal dopamine alterations, specifically how dopaminergic dysfunction drives maladaptive phenotypes such as

hyperactivity and anxiety remains unclear. This study aims to identify the dopaminergic populations driving anorexic phenotypes in the ABA model by chemogenetically targeting dopaminergic neurons in the ventral tegmental area (VTA) and substantia nigra (SN) of Th:Cre rats. We hypothesize that dopaminergic activation will increase hyperactivity, while inhibition will mitigate the development of anorexic behaviors. We show that VTA dopamine activation during ABA significantly increases light-phase running wheel activity (n=19, $F(2,16)=37.9$, $p<0.0001$, Tukey's post hoc: $p=0.0011$) without affecting food intake or body weight. In contrast, VTA dopamine inhibition reduces light-phase hyperactivity ($p=0.0082$). Additionally, VTA dopamine activation increases time spent in the open arms of the elevated plus maze test, suggesting a potential link to anxiety-like behavior. These results indicate that VTA dopamine neurons contribute to both hyperactivity in the ABA model and anxiety. Ongoing research aims to further differentiate the roles of VTA and SN dopamine populations as well as dissect specific VTA projections contributing to hyperactivity and anxiety.

P338 **Novel Insights Into The Neurobiological Basis Of Anorexia Nervosa: Role Of Oxytocin In The *Anx/Anx* Mouse Model**

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Anorexia nervosa (AN) is a severe psychiatric disorder with high mortality and relapse rates, associated with altered hypothalamic neuropeptide signaling. Among these peptides, oxytocin (Oxt) has emerged as a key regulator of energy balance, stress responses, and social behavior. The paraventricular (PVN) and supraoptic (SON) nuclei, major sites of Oxt synthesis, modulate these critical functions frequently disrupted in AN and other psychiatric disorders. Given the known alterations of the oxytocinergic and olfactory systems in psychiatric conditions, we aimed to investigate the possible role of the central oxytocinergic system in the neurobiology of AN.
We used the anx/anx mouse as a preclinical model of AN, and wild-type sibling mice as a control group. Immunofluorescence assessed Oxt and Oxt receptor expression in hypothalamic and olfactory areas; also, neurohypophysial and plasma Oxt were measured. Whole transcriptomic profiles of PVN and SON were evaluated. Immunofluorescence (n=6/group) and plasma (n=6/group) data underwent Student's t-test or Mann-Whitney, according to data distribution. For transcriptomic differential expression analysis (PVN, SON; n=4/group) were used empirical Bayes moderated t-statistics with Benjamini–Hochberg correction (FDR<0.05).
Our data show an overall alteration of the oxytocinergic signaling in brain areas related to olfaction, particularly an overall high immunoreactivity of the Oxt receptor in anorectic mice.
From spatial transcriptomic analysis, we identified differentially expressed genes in PVN and SON most involved in neuronal plasticity and microglia activation.
Our findings highlight dysfunctions in the oxytocinergic and olfactory systems in AN, providing novel insights into its neurobiology and suggesting a novel therapeutic target for this severe psychiatric condition.

P340 **The Role Of Hindbrain Gfral Neurons In The Mediation Of Nausea, Emesis And Anorexia**

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Growth differentiation factor 15 (GDF15) is a stress cytokine that binds to GDNF family receptor α–like (GFRAL) in the area postrema (AP) and nucleus tractus solitarius (NTS), two key hindbrain regions involved in regulating feeding behavior and malaise. GDF15 has been shown to reduce food intake and body weight, and recent studies indicate that its potent anorectic effects are primarily mediated through the induction of nausea and emesis. Elevated endogenous GDF15 levels are linked to various diseases and treatments characterized by nausea and vomiting, including chemotherapy. Despite existing antiemetics, nausea and vomiting remain poorly managed in these conditions, often ranking as the most distressing side effect of treatments and leading to treatment discontinuation. The role of GDF15/GFRAL signaling in sickness-related anorexia and nausea tied to these conditions, however, remains unclear. Here, we investigate whether blocking GDF15/GFRAL signaling can alleviate nausea and anorexia associated with the highly emetic chemotherapeutic agent cisplatin in rats. We show that cisplatin causes an increase in GDF15 plasma levels and activation of GFRAL neurons. Pretreatment with a GFRAL antagonist significantly attenuates behaviors indicative of malaise (i.e., anorexia and pica behavior) caused by cisplatin. Additionally, GFRAL antagonism significantly reduced cisplatin-induced neuronal activation in both the AP and NTS. Together, these results indicate that $GFRAL^+$ neurons play an important role in mediating chemotherapy-induced visceral malaise and their pharmacological inhibition shows potential as a therapeutic approach to alleviate these side effects. This work was partially supported by the Pfizer Competitive Grant Program.

P342 **Serotonin Neurons Are Necessary For Tonic Sodium Intake Inhibition.**

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Sodium appetite is a motivated behavior that occurs in response to sodium deprivation. Various neurotransmitters, including serotonin, are thought to regulate sodium intake. In the present study, we used genetic deletion to test whether serotonergic neurons are necessary for regulating sodium appetite. First, we confirmed that Pet1-Cre; Lmx1bflox/flox (Lmx1bf/f/p) mice have nearly complete deletion of serotonergic neurons, with only sporadic cells remaining. Next, we measured baseline intake of water and 3% NaCl and found that Lmx1bf/f/p mice consume more salt than Cre-negative littermates (Lmx1bf/f) on a low-sodium diet. Finally, we tested the necessity of serotonergic neurons for thirst and sodium appetite inhibition in three experimental paradigms. After 24-hour water deprivation, mice lacking serotonergic neurons exhibited an intact thirst response by increasing water intake similar to Cre-negative littermates. After furosemide diuresis and 24-hour sodium deprivation, mice lacking serotonergic neurons exhibited an intact sodium appetite response by increasing sodium and water intake consumption like Cre-negative littermates. After six days of dietary sodium deprivation, mice lacking serotonergic neurons increased sodium and water intake more than Cre-negative littermates. Together, these findings indicate that while serotonergic neurons are not the primary mechanism controlling sodium appetite, they act as a physiological 'brake' that limits sodium consumption across multiple contexts. This tonic inhibitory role may protect against excess sodium intake and

raises the possibility that serotonergic medications may influence dietary sodium consumption.

P344 **Relaxin-3 Signaling In The Nucleus Tractus Solitarius Induces Hyperphagia And Insulin Resistance**

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Relaxin-3 is an orexigenic neuropeptide produced principally by neurons in the nucleus incertus (NI) of the hindbrain which project widely throughout the brain. The majority of relaxin-3 fibers project to midbrain and forebrain regions with established roles in modulating arousal, stress, and memory in addition to feeding. However, a population of relaxin-3 neurons project posteriorly to the nucleus tractus solitarius (NTS) of the hindbrain, the physiological function of which has yet to be described. Given the critical role of the NTS in energy balance control, we investigated the impact of hindbrain-targeted relaxin-3 signaling on appetite and metabolic regulation. We first confirmed that the NTS expressed the relaxin-3 receptor (rxfp3) using fluorescent in situ hybridization, which were most abundantly expressed on GABAergic neurons. We observed close proximity of relaxin-3 positive fibers to rxfp3 expressing cells in the NTS, and injection of the retrograde tracer fluorogold in the NTS colocalized with relxin-3 positive soma in the NI, supporting a functional NI-to-NTS circuit. Fourth ventricle injection of relaxin-3 elevated intake of chow and high-fat diet in rats, consistent with its orexigenic function described in the hypothalamus. Additionally, hindbrain-targeted relaxin-3 worsened insulin sensitivity during an insulin tolerance test. As NI relaxin-3 expression is chronically elevated in diet-induced obese rats, increased signaling in the NTS may contribute to the hyperphagia and metabolic dysfunction of obesity. Future work will explore where NTS rxfp3 neurons project to and the contribution to this population to energy balance regulation in the face of metabolic challenges.

P346 **Investigated The Influence Of Hunger Sensing Neuron In Motivation And Learning Behaviour**

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Hunger sensing AgRP neurons respond to periods of energy shortage and are crucial for maintaining food-seeking behaviour including increasing motivation, learning, memory, and reducing anxiety. Whether acute stimulation linked to food delivery drive food-seeking behaviour remains unknown. The impact of brief AgRP stimulation on food-seeking behaviour under extinction conditions in the absence of food reinforcement or during reversal learning has not been examined. We hypothesise that brief close-loop time locked optogenetic control of AgRP neurons link to food retrieval differently affects motivation, extinction and reversal learning. Brief time-locked optogenetic stimulation or inhibition of AgRP neurons was delivered in response to food retrieval with FED3, which closely examine the relationship between neuronal activity and animal behaviour. Behaviours included motivated food seeking during a progressive ratio, food-seeking under conditions of reversal learning and during extinction in the absence of food reinforcement. Constant AgRP neuronal activation increased motivating food seeking, delayed extinction and increased reversal learning on days 2 and 3 after the previously inactive right poke became the active poke delivering food. Both short-term closed and open loop AgRP stimulation increased motivated food-seeking indicating brief AgRP stimulation does not need to be linked to food retrieval to motivated food seeking (n=11-20). Closed-loop stimulation also delayed extinction but increased reversal learning on days 2 and 3. Our results indicate that brief AgRP activation affects food-seeking behaviour independent from behaviour. Understanding how these neurons regulate behaviour is important to understanding conditions that affect excessive or reduced food intake.

P348 **Mu Opioid Receptor Regulation Of Motivation And Learning In Orbitofrontal Cortex**

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The orbitofrontal cortex (OFC) is critical for complex reward valuation and action-outcome associations. Previous work using pharmacological microinjections in rats has shown that mu-opioid receptor (MOPR) stimulation in the OFC enhances food intake. However, whether MOPRs in the OFC influence classical or operant conditioning remains untested. We hypothesized that if MOPRs in the OFC regulate reward valuation, their selective disruption would reduce both unconditioned and conditioned motivated behaviors by impairing the ability to appropriately attribute value to rewarding stimuli. Using a conditional knockout (cKO) mouse model (n = 7 control, n = 10 experimental), we selectively deleted MOPRs in the OFC and assessed behaviors including unconditioned sucrose intake, classical conditioning, operant self-administration (FR1, FR3), progressive ratio (PR), and reversal learning. Mice with MOPR deletion in the OFC showed reduced *ad libitum* and food-deprived sucrose intake but no deficits in classical conditioning (e.g., latency to food port after cue, CS+ vs. CS- discrimination) or FR1/FR3 acquisition. However, these mice exhibited a significantly lower PR breakpoint, suggesting reduced motivation to work for rewards under increasing effort demands. Furthermore, cKO mice failed to acquire operant reversal learning, even after six days of training, indicating a specific deficit in adapting to changes in reward contingencies. These findings provide the first evidence that MOPRs in the OFC are necessary for unconditioned and operant conditioned motivated behaviors and are particularly integral for reversal learning, but not basic contingency learning. Future work will examine whether these effects are driven by specific subregions or cell types in the OFC.

P350 **Glucagon-Like Peptide-1 Receptor Activation Influences Excitatory Dynamics In Piriform Cortex Pyramidal Neurons**

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Olfactory cues in the environment can signal food availability and drive food-seeking behaviors. At the same time, physiological changes, such as in satiety, can dampen the potency of olfactory cues on motivated behaviors. The satiety factor, glucagon-like peptide 1 (GLP-1), modulates the activity of olfactory bulb (OB) output cells. However, very little is known regarding the effects of GLP-1 signaling on the piriform cortex (PC), where odor identities and associations to food are established. Therefore, we hypothesized that hindbrain GLP-1 neurons in the nucleus of the solitary tract (NTS) project to the PC, where they can modulate pyramidal cell excitability. We injected a retrograde fluorescent tracer, cholera toxin subunit b (CTb), into the PC. We observed neurons containing CTb in the NTS, thereby indicating a direct connection between the NTS and PC. We then hypothesized that GLP-1 receptor (GLP-1R) agonism would modulate synaptic signaling

within the PC. Using patch clamp electrophysiology, we found that while direct GLP-1R agonism (Exendin-4, 1 μM) did not change the cell-intrinsic rheobase, it did increase excitatory drive to the PC pyramidal neurons by increasing spontaneous excitatory postsynaptic current frequency (EPSC; $\beta = 4.17$, $p < 0.01$), increasing spontaneous EPSC magnitude ($\beta = 39.45$, $p < 0.01$), and decreasing evoked inhibitory postsynaptic current magnitude ($t = 3.15$, $p = 0.02$). Our data suggest the possibility of NTS GLP-1 neurons projecting to the PC, where they modulate olfactory processing. Ongoing experiments using in vivo imaging of OB output neurons (which receive PC input) will reveal their neural responses to food odors in anesthetized animals that have either been fed adlib, food-restricted, or have been injected with a GLP-1R agonist.

P352 **Hippocampal Metabolic Abnormalities Following Western Diet Consumption In A Mouse Model**

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Western diets containing saturated fats and sugars are detrimental to the hippocampus, a brain region involved in learning and memory. However, mechanisms for WD-induced hippocampal dysfunction remain unclear. We hypothesized that WD consumption would negatively impact hippocampal cellular metabolism which is critical for neurobiological function. To investigate this, we randomized adult male (n=36) and female (n=32) C57BL/6J mice to receive a control (standard chow + water) or WD (chow with 60% kcal from fat + 11% high fructose corn syrup solution). Mice were assessed for peripheral metabolic changes and hippocampal-dependent learning and memory function, and hippocampi were dissected for cell-type specific RNA sequencing and mitochondrial functional assays. Statistical analyses used were two-way ANOVA for body weight and student's t-test for all other analyses. Benjamin-Hochberg adjusted false-discovery rate was used for differently expressed genes (DEGs). Male WD mice demonstrated impaired hippocampal function in the Y maze spatial memory task. Both sexes had an increase in fat percentage and blood glucose area under the curve assessed via body composition scans and glucose tolerance tests, respectively. Gene Ontology Pathways analysis of DEGs in hippocampal tissues demonstrated an increase in pathways related to mitochondrial function in neurons, corresponding with decreased activity and electron conductance of complex I of the electron transport chain. Taken together, these findings suggest that WD consumption has profound metabolic impacts within the hippocampus. As complex 1 dysfunction promotes neurodegenerative disease and cognitive dysfunction, we propose that WD-induced metabolic dysfunction may be causally related to hippocampal impairments.

P354 **Sex Differences In Obesity Resistance And Dietary Fat Preferences**

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High-fat diets (HFD) are increasingly prevalent in modern diets, heavily contributing to the global rise in obesity and metabolic dysfunction. While animal-based HFD (anim-HFD) has been extensively studied, the metabolic and behavioral impacts of vegetable-based HFD (veg-HFD) remain poorly understood, despite the growing use of vegetable oils and plant-based foods. Furthermore, biological sex plays a critical but understudied role in feeding behavior and obesity susceptibility. Here, we investigate how exposure to varying combinations of SD, anim-HFD, and veg-HFD influences feeding behavior, standard diet (SD) devaluation, and food preference across sexes in mice. We discovered that exposure to veg-HFD leads to similar levels of SD devaluation as that observed followed chronic anim-HFD access, suggesting that vegetable-based fats are potentially as obesogenic as anim-HFDs. Across both HFD types, female mice displayed a higher resistance to HFD-induced weight gain and SD devaluation, suggesting a potential protective effect against obesity. Ongoing analysis of neural ensemble activity, including in hunger-promoting agouti-related peptide (AgRP) neurons, following anim-HFD, veg-HFD, or a combination of these diets across sexes is ongoing, with the hope to identify unique neural markers of diet preference in female versus male mice. These results highlight the importance of dietary composition and biological sex in shaping feeding behavior and obesity risk, with implications for developing sex-specific dietary interventions.

P356 **Sex Difference In Enhancement Of Conditioned Taste Aversion Learning By Systemic Hdac Inhibitors Butyrate And Valproate**

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Histone acetylation is a chromatin modification which regulates gene expression and has been shown to play a role in learning and memory. Inhibition of histone decetylases (HDACs) can enhance the magnitude and prolong extinction of conditioned taste aversion (CTA), e.g., after systemic butyrate (Kwon and Houpt, 2010). To determine if the CTA enhancement by systemic butyrate generalized to another short-chain fatty-acid HDAC, the effects of butyrate (400 mg/kg) administered after the pairing of saccharin and LiCl (38 mg/kg) was compared to the systemic valproate (100mg/kg) administered prior to saccharin-LiCl pairing in rats (n=6-8 per group). Magnitude and extinction of the CTA was measured with 10-14 days of 2-bottle preference tests. Both butyrate and valproate enhanced CTA in male but not female rats. As a preliminary investigation of the role of gonadal hormones in the observed sex difference, butyrate was administered after saccharin-LiCl pairing to intact and ovariectomized female rats, and to intact and orchiectomized male rats. Butyrate did not enhance CTA learning in either group of female rats. However, butyrate enhanced CTA learning in intact male rats, but not in orchiectomized rats. These results suggest that testosterone may contribute to the sensitivity of male rats to HDAC inhibition.

P358 **Leptin Effects On Primary Cilia And Energy Homeostasis**

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Leptin, an adipose-derived hormone that modulates energy homeostasis, acts in the brain to reduce food intake, a process requiring leptin receptor containing neurons of the

ventromedial hypothalamus (VMH). Neurons of the VMH contain primary cilia, antenna-like structures that house G-protein coupled receptors (GPCRs), whose downstream signaling effects are mediated by adenylyl cyclase 3 (AC3). Hypothalamic primary cilia length and/or expression of AC3 modulates body weight, and leptin has been suggested to elongate hypothalamic primary cilia. We hypothesize that leptin reductions in food intake involve an elongation of AC3 positive primary cilia in the VMH. Immunofluorescent staining results show that peripheral leptin injection at a dose sufficient to reduce food intake and elevate pSTAT3 in the VMH also elongates AC3-positive cilia in these cells (Student's T tests; $P<.05$). VMH AC3 positive neurons contain the somatostatin 3 receptor (SSTR3), but not the melanin concentrating hormone receptor 1. To determine whether an anorexigenic dose of leptin increases AC3 loading onto the cilium or elongates the whole cilium, we double labeled cilia with SSTR3 and AC3 in rodents injected with a 4th ventricle anorexigenic dose of leptin (2 μg) or vehicle (n=8/group). Ongoing research is investigating whether AC3 signaling in the VMH is critical for leptin mediated modulation of body weight. Understanding the role of primary cilia in leptin regulation of energy balance may be key to understanding mechanisms underlying leptin sensitivity.

P360 **Reward-Specific Satiety And Reward-Specific Motivation: Neural Bases**

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Reward-specific satiety (or sensory-specific satiety) is the sensory-specific decrease in the reward value and pleasantness of a particular reward such as a particular food when it is consumed to satiety. Reward-specific motivation (or incentive motivation) is the increase in the reward value of a reward when it is first consumed. These are some of the most powerful influences on what is eaten and how much in a meal. Sensory-specific satiety was discovered (in 1981, see Rolls, 2015) when recording from single neurons in primates, and has been shown to be a property of neurons and human fMRI activations in the orbitofrontal cortex but not in the insular primary taste cortex or inferior temporal visual cortex that send taste and visual inputs to the orbitofrontal cortex. Here I propose that the neural basis of reward-specific (or sensory-specific) satiety is synaptic adaptation in the synapses on to orbitofrontal cortex reward value neurons in humans and other primates; and that reward-specific motivation (or incentive motivation) is shorter term synaptic facilitation in the same synapses on to orbitofrontal cortex reward value neurons. This theory is elucidated by integrate-and-fire neuronal network models of how these computations are performed in the orbitofrontal cortex to implement a profound influence on behavioural choice, of for example food, that has great adaptive value. This is the first theory of how reward-specific satiety and reward-specific motivation are computed in the brain. Rolls, E. T. (2016) Reward systems in the brain and nutrition. Annual Review of Nutrition 36: 435-470. Rolls, E. T. (2023) Emotion, motivation, decision-making, the orbitofrontal cortex, anterior cingulate cortex, and the amygdala. Brain Structure and Function 228: 1201-1257.

P362 **Melanin-Concentrating Hormone Expressing Cells In The Lateral Hypothalamus But Not The Zona Incerta Increase Water Consumption In Male And Female Rats.**

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Melanin-concentrating hormone (MCH) is a neuropeptide primarily produced in the lateral hypothalamus (LHA) and the zona incerta (ZI). MCH increases energy conservation by increasing caloric intake as well as decreasing energy expenditure. Previous work also links MCH activity with water consumption. It is unclear, however, whether it is the LHA or the ZI population of MCH neurons that drives water consumption. Additionally, it is unknown which efferent nuclei the MCH neurons are communicating with to influence thirst. To further characterize the mechanisms through which MCH promotes water intake, we combined behavioral analyses with MCH neuron-specific designer receptors exclusively activated by designer drugs (DREADDs). An AAV driving expression of an excitatory DREADD (MCH-hM3Dq-mCherry) under the control of an MCH promoter was injected into either the LHA or the ZI of adult male and female rats (n=28). We used the DREADD agonist DCZ to activate LHA^{MCH} or ZI^{MCH} neurons during the onset of the rats' light cycle with free access to water but not chow. Our results revealed that LHA^{MCH}, but not ZI^{MCH}, stimulation significantly increased water licking, driven by an increase in licking burst number. Ongoing experiments build on these findings to identify potential neural circuit targets of LHA^{MCH} neurons by looking at axonal expression of mCherry, as well as subsequent Fos expression in downstream nuclei stimulated by MCH-hM3Dq-mCherry-mediated activation. These studies add to the growing body of literature implicating MCH in driving thirst and ingestive behavior more broadly.

P366 **Optogenetic Stimulation Of Cck Neurons Activates Nts Neurons Via Glutamate And Cck Release.**

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Cholecystokinin (CCK) is a satiety peptide that is released from the gut following ingestion of primarily fats and peptides. It binds to CCK 1 receptors (CCK1Rs) expressed on peripheral vagal afferent terminals, leading to their activation and a decrease in food intake. Additionally, CCK1Rs are also expressed on central vagal afferent terminals, which form direct synapses with neurons in the nucleus of the solitary tract (NTS). Activation of these central CCK1Rs increases c-fos expression in NTS neurons and decreases food intake in male rats. However, sources of CCK that may act on central CCK1Rs and the effects of activating central CCK1Rs in females remains understudied. We hypothesize that a subpopulation of NTS neurons that express CCK as well as descending fibers from the forebrain may serve as a local source of CCK. Here, we expressed channel rhodopsin (ChR) in CCK neurons of male and female mice and recorded electrophysiological activity while performing photostimulation. We found that CCK neurons form connections with NTS neurons and that glutamate release from their terminals is sufficient to activate other NTS neurons. We also found that high

frequency photostimulation leads to a sustained increased in spontaneous EPSC frequency, which closely mimics the effects of bath applying CCK in the NTS and was blocked by a CCK1R antagonist. To further characterize the *in-vivo* effects of central CCK1R activation, we next administered a CCK1R agonist into the fourth ventricle of male and female rats, which resulted in a decrease in food intake as well as increased c-fos expression in NTS neurons. Taken together with previous research, these findings suggest that CCK neurons activate NTS neurons via both glutamate and CCK release, which is sufficient to alter food intake.

P368 **Relationship Between Blood Sugar Excursions And Cravings For Ultra-Processed Rewarding Food In Healthy Adults**

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In obesogenic environments, ubiquitous ultra-processed rewarding food (UPRF) cues may trigger cravings, typically regulated by inhibitory control. However, the role of glycemia regulation in UPRF cravings is underexplored. We examined the influence of post-meal glycemia on neurocognitive and behavioral craving correlates. We hypothesized that glycemic spikes from a carb-rich, low-protein and fiber (HCLPF) meal will increase UPRF cravings and *ad libitum* food consumption compared to a Mediterranean-style (MED) balanced meal. Methods: In a crossover design, 14 healthy adults consumed isocaloric HCLPF and MED breakfasts, with counterbalanced order and a one-wk washout. Before visits, they followed a 24 hr standardized diet and fasted overnight to regulate hunger and intensify cravings. During visits, blood glucose was measured at T0 (pre-meal), and T1 (30 min) and T2 (60 min) post-breakfast. At T1, participants completed a Food Stroop task assessing attentional bias to UPRF images. At T2, a Saliva Magnitude Test (SMT) with baked goods warming nearby (as a salient food cue) was followed by an *ad libitum* preference-tailored UPRF buffet. Results: Blood sugar levels rose similarly from T0 to T1 for both meals but were significantly higher after HCLPF than MED from T1 to T2. Salivation and buffet intake were similar across meals. However, regression analysis indicated that post-HCLPF glycemia and salivation uniquely predicted attentional bias, controlling for age and gender. No such patterns emerged after MED. Conclusions: Post-HCLPF glycemia and salivation were linked to attentional bias toward UPRF cues, but not to increased food buffet intake. Further study of glycemic mechanisms in UPRF cravings may inform overeating interventions.

P370 **Hdac6, Leptin, The Brain, And Energy Partitioning.**

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The central nervous system plays a crucial role in regulating energy metabolism, yet the mechanisms governing body composition and energy partitioning between adipose tissue and muscle remain incompletely understood. Here, we demonstrate that neuronal HDAC6 modulates body composition, particularly under obesogenic conditions. Neuron-specific HDAC6 knockout mice (HDAC6Δbrain) exhibit comparable weight gain to controls when exposed to a high-fat diet but preferentially accumulate lean mass over fat mass and display elevated energy expenditure. Despite increased food intake, HDAC6Δbrain mice retain leptin sensitivity, which can be normalized with exogenous leptin administration. However, HDAC6 does not regulate leptin signaling in a cell-autonomous manner. Instead,HDAC6Δbrain mice maintain leptin sensitivity primarily due to relative hypoleptinemia. Consistently, lean HDAC6Δbrain mice and global HDAC6 knockout mice—both with normal body composition and leptin levels—do not exhibit enhanced leptin sensitivity. To further dissect the role of central HDAC6, we leveraged the pharmacological properties of brain-penetrant and peripherally restricted HDAC6 inhibitors. Our in vivo studies reveal that while both inhibitors promote weight loss in diet-induced obese mice, the brain-penetrant inhibitor more effectively prevents adiposity with a consequent reduction in circulating leptin levels. All experimental groups consisteded of n=8-12 animals. Student's test, 1 or 2-way ANOVA was used to calculate statistical significance. These findings establish HDAC6 as a key regulator of energy partitioning and suggest that targeting central HDAC6 may offer a novel strategy to prevent the onset of leptin resistance and metabolic dysfunction.

P372 **Endocannabinoid Signaling To Astrocytes In The Hypothalamus Modulates Feeding Behavior And Energy Metabolism.**

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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 Ca^{2+} 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, exclusively in males. 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 in a sex-dependent manner.

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Perinatal High-Fat Diet Induces Systemic Inflammation And Disorganization Of Colonic Tight Junction Protein Complexes During Development

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Rat offspring of dams fed a high-fat (HF) diet during gestation and lactation have altered feeding behavior and are more susceptible to obesity. Prior data from our lab show that maternal high-fat diet (mHFD) results in increased GI permeability and gut dysbiosis at weaning on postnatal day (P)21. We hypothesized that by P21, HF offspring have altered organization of intestinal tight junction proteins resulting in increased permeability and greater circulating inflammatory factors. Timed-pregnant Sprague Dawley rats were fed either standard laboratory chow (CH) diet (13% kcal fat) or a purified HF diet (60% kcal fat) during gestation and lactation (n = 7-8/diet). On P21, plasma was collected from male and female pups for quantification of circulating proinflammatory cytokines and LPS. Colonic tissue was collected at P21 for Western blot (WB) and immunofluorescent (IF) staining of tight junction (TJ) proteins: Claudin-1 (CLDN-1), Occludin (OCLN), and Zonula Occludens-1 (ZO-1), involved in regulating paracellular permeability. There was an overall effect of mHFD increasing plasma IL-1β($P < 0.005$), in male (CH 0.2 ± 0.1 vs. HF 1.4 ± 0.6 pg/mL) and female (CH 0.8 ± 0.4 vs. HF 2.1 ± 0.6 pg/mL) offspring. While there was no effect of mHFD on plasma LPS, there was a significant sex effect ($P < 0.005$) with males having increased LPS levels compared to females at P21. There were no differences in total colonic TJ protein levels measured by WB, but IF showed HF male offspring had significantly decreased colocalization between CLDN-1 and ZO-1 ($P < 0.05$) indicating disorganization of colonic TJ protein complexes only in males. These findings point to a potential sex-specific mechanism by which mHFD exposure induces systemic inflammation during a critical period of development.

P376

Knockdown Of Hypothalamic Astrocyte Ketogenesis Impairs Energy Expenditure And Thermogenesis

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Specialised neurons in the mediobasal hypothalamus (MBH) detect metabolic signals to coordinate processes such as food intake and energy expenditure. Growing evidence suggests that MBH astrocytes support and modulate neuronal-nutrient sensing. In response to high-fat diet (HFD) exposure and fatty acid (FA) excess, hypothalamic astrocytes become ketogenic. Pharmacological inhibition of MBH ketogenesis significantly blunted anorectic responses to acute HFD exposure in both wild-type and diet-resistant rats. Thus, astrocyte-derived ketone signalling has been proposed to modulate neuronal nutrient sensing as a protective mechanism against HFD exposure. To investigate this hypothesis, our group explored the metabolic role of MBH astrocyte FA transporter 4 (FATP4) and ketogenic enzyme HMG-CoA lyase (HMGCL) in mice and rats, respectively. A GFAP-specific Cre-expressing AAV was stereotactically delivered into the MBH of $FATP4^{fl/fl}$ mice. When fed a 45% HFD, knockout mice gained significantly more weight than controls. Interestingly, this increase in body weight was not due to sustained changes in food intake - which only rose during the first week of HFD - but was instead driven by alterations in energy expenditure. These changes were associated with reduced core body temperature and brown adipose tissue oxidation. Knockdown of HMGCL in the MBH astrocytes of Sprague-Dawley rats promoted similar effects, increasing body weight, reducing energy expenditure and impairing thermogenesis. Overall, these findings highlight the role of astrocytes in the maintenance of energy homeostasis. Future experiments will aim to identify which neuronal populations are targeted by astrocyte-derived ketone body signalling and to identify the intracellular mechanisms underlying this interaction.

P378

Hypophagia And Body Weight Loss By Tirzepatide Are Accompanied By Fewer Gi Adverse Events Compared To Semaglutide In Preclinical Models

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Glucagon-like peptide 1 receptor (GLP-1R) agonists improve glycemic control and reduce food intake, providing a minimally invasive treatment for individuals with obesity and/or type 2 diabetes; however, this often coincides with side effects such as nausea and vomiting, impacting treatment adherence and quality of life. Until recently, GLP-1's sister incretin, glucose-dependent insulinotropic polypeptide (GIP), has been overlooked as a treatment for obesity since its hypophagic effects are weak compared to GLP-1R agonists. However, GIP receptor (GIPR) agonism when combined with GLP-1R agonists, has yielded superior results in enhancing glycemic control and weight management compared to GLP-1R agonism alone. Intriguingly, GIPR agonism appears to induce antiemetic effects, potentially alleviating part of the nausea and vomiting side effects common to GLP-1R agonists like semaglutide. Here, we show in rats and musk shrews that GIPR agonism blocks emesis and attenuates other malaise behaviors elicited by GLP-1R activation, while maintaining reduced food intake, body weight loss, and improved glucose tolerance. Importantly, the GLP-1R/GIPR agonist tirzepatide induced significantly fewer side effects than equipotent doses of semaglutide. These findings highlight the potential of combined pharmaceutical strategies activating both incretin systems, leading to enhanced therapeutic index and reduced occurrence of nausea and vomiting for obesity and diabetes treatments.

P380 **Mild Protein Restriction At Thermoneutrality Uncouples The Feeding, Metabolic And Food Preference Responses To Protein Dilution.**

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The protein leverage hypothesis provides a conceptual framework resolving the consequences of reduced dietary protein intake on appetite and weight gain, a mechanism potentially contributing to the obesity epidemic. However, existing murine models of protein restriction fail to validate key aspects of the protein leverage hypothesis, limiting progress in the identification of the neuronal mechanisms regulating appetite and energy balance in contexts where animals mount successful adaptive strategies to maintain protein balance without trade-off. Here we provide new evidence that mice regulate their protein intake independently of energy intake to reach an average of 1.9kCal protein per day. Mild protein restriction, providing 10% of energy as protein, produces hyperphagia independently of changes in energy expenditure, leading to increased adiposity, and protein preference. Unexpectedly, this hyperphagic response is blunted at thermoneutrality, leading to loss of lean mass and body weight. Likewise, protein-restricted mice failed to exhibit protein preference at thermoneutrality. Under these conditions, mice are unable to defend postabsorptive circulating levels of essential amino acids, which are normally tightly regulated in mice fed low protein diets at room temperature. Metabolomics and transcriptomics analysis revealed critical roles for hepatic and brown fat amino acid catabolic pathways in amino acid homeostasis, blunted at thermoneutrality. Thus, housing temperature determines the feeding and metabolic consequences of mild protein restriction and the efficiency of metabolic pathways buffering circulating levels of essential amino acids.

P382 **Adult Hypothalamic Oligodendrogenesis Tracks Time-Of-Day To Regulate Energy Balance**

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Due to the significant daily environmental changes associated with the ~24-hour rotation of the earth around its axis, most animals have evolved an internal timing system known as the circadian clock to anticipate and adapt to the recurring variations. In mammals, the hypothalamic suprachiasmatic nucleus (SCN) serves as the master pacemaker which tracks time-of-day and keeps physiology and behaviour in synchrony with the day-night cycle. Food intake is one of the main aspects of physiology regulated by the circadian clock. However, how the brain master clock modulates energy balance is not fully understood. Recently, adult oligodendrogenesis in the median eminence (ME), a circumventricular organ bordering the arcuate nucleus of the mediobasal hypothalamus, has been shown to response to the body's nutritional states and play a key role in regulating energy homeostasis. Also, the ME receives dense projections from the SCN. Thus, we hypothesise that the SCN circadian clock regulates brain circuits for feeding and metabolism, via oligodendrocytes (OLs), a type of non-neuronal cells in the brain. Using in vivo EdU proliferation assay on mouse models, we showed that oligodendrogenesis in the ME uniquely exhibits strong diurnal rhythms – which are abolished by 1-week mistimed feeding, leading to a net loss of ME OLs. Further investigations revealed the SCN-AVP neurons negatively regulate ME OL lineage progression. Transgenic mouse models with blunted adult oligodendrogenesis showed dampened diurnal feeding and metabolic rhythms. Together, our results indicate a novel neural mechanism though which the SCN master clock regulates circadian timing of energy balance. Future works will focus on elucidating the molecular underpinnings and the physiological importance of this novel circuit.

P384 **Portion Size Influences Intake Of A Highly Valued Traditional Food In Samburu People Of Rural Kenya**

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The Samburu are a semi-nomadic, pastoralist people in rural Kenya who have little exposure to the modern food environment and whose traditional diet and distinctive social norms for eating differ dramatically from Western cultures. In previous work on meal size and satiety in Samburu we observed a rather strong portion size effect in both men and women, whereby larger portions stimulated larger meals apparently without awareness. However that study used a test food which, although familiar and acceptable, was not a preferred, traditional food, thus the result may not represent typical behavior. Here we report new experiments testing for a portion size effect using milk and meat, two high-value foods integral to their traditional diet. When provided a meal that was relatively smaller or larger (yet always more than a participant could finish) both men and women consumed significantly more meat when served a larger amount, a striking result given a powerful social norm that encourages eating meat to maximal capacity. Yet in two experiments with milk, another preferred traditional food, neither portion size nor drinking vessel size influenced intake. These experiments demonstrate the portion size effect remains a powerful influence on intake for Samburu people even when eating a high-value food and striving for maximal consumption. But the effect may not occur with all foods, potentially attributable to properties of the food itself (e.g., liquid or solid), aspects of the meal (e.g., duration), or culturally-specific cognitions or norms about the food.

3:00 - 4:30 PM	L2
Symposium 4: It is all in the blend: Effects of combining macronutrients on food intake and reward	

Chair(s): Anne Roefs

3:00 **Why Do Humans Blend Macronutrients?**

Annika N. Flynn[1], Peter J. Rogers[1], Mark Schatzker[2], Jeffrey M. Brunstrom[1]

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Foods with a more equal blend of energy from carbohydrate and fat are found to be more rewarding. Previously, we hypothesised that the underlying mechanism is *reduced* satiety – these 'combo' foods deliver *less* satiety per calorie (i.e., have a higher energy-to-satiety ratio). Thus, combo foods are more rewarding because they facilitate energy intake – the goal of eating is to ingest nutrients, not to achieve satiety. Consistent with this hypothesis, our work shows that combo foods are (1) more palatable, (2) more rewarding, and (3) less satiating. More recently, we have become interested in how energy-to-satiety ratio might influence everyday dietary behaviours and whether humans strategically combine foods to form a meal (*e.g.*, cheeseburger and fries). Taken together, I will suggest that these real-world preferences and decisions can be interpreted through the lens of optimal foraging.

3:30 **All Mixed Up: A Sensory Scientist&Rsquo;S View Of Foodï¿½Formulation And Eating Behavior.**

John Hayes[1,2]

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Discussions of formulation and eating behavior are implicitly mediated via sensation and affective responses. Dr. Hayes will review the putative causal chain linking formulation to intake in humans, including some logical fallacies and empirical data that challenge this common framework. Insights on cross modal interactions, mixture suppression, the bliss point, and individual differences will be discussed within the context of food reformulation.

4:00 **Reinforcing Properties Of Hyper-Palatable Foods And Within-Meal Energy Intake**

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Rationale/premise: A definition of hyper-palatable foods (HPF) was developed in 2019 and specifies quantitative combinations of nutrients (fat and sodium; fat and sugar; carbohydrates and sodium) at thresholds not found in nature. The nutrient pairs in HPF are hypothesized to be a mechanism that yield acute rewarding effects during consumption, which can lead to overeating, and garner strong wanting and drive to consume HPF. Research using multiple methodologies has tested these hypotheses. Methods: Study 1 used an experimental paradigm with N=339 participants online to test the acute rewarding and behavioral reinforcing properties of HPF with elevated sodium, relative to matched foods without sodium (non-HPF). Study 2 used smartphone-based remote food photography methodology to assess the role of HPF in within meal energy intake among N=29 participants who reported 345 total eating occasions in free-living conditions. Results: Study 1: HPF were significantly more liked and more desired (wanted), relative to matched foods without sodium, with large effects (η^2 = .56-.68, p-values <.001). Participants were willing to pay more for HPF relative to matched items without sodium (η^2=.17, p <.001), indicating HPF were more strongly valued as rewards. Study 2: Bayesian mixed models indicated that when participants consumed greater %kcal from HPF in eating occasions than their average, they consumed greater total kcal during the eating occasions (Median β = 0.09, pd = 99.56%), and post-meal endorsed greater eating despite feeling full (Median β = 0.15, pd = 96.45%), when accounting for hunger and energy density. Conclusions: HPF were liked and wanted more, and were valued more as rewards than matched foods without sodium (non-HPF), indicating their strong reinforcing properties and highlighting the role of sodium in their reinforcing effects. Findings from the free-living study identified the role of HPF themselves in within-meal energy intake, distinct from individual-level differences in HPF intake.

3:00 - 4:30 PM	L1
Oral Session 6: Treatments & Interventions for Disregulated Ingestive Behaviors	

Chair(s): Tito Borner

3:00 **Reduced Subjective Valuation Of High-Caloric Density Foods After Bariatric Surgery: Associations With Appetite Regulating Hormones (New Investigator Travel Awardee)**

Patrick Gagnon[1,2,3], Justine Daoust[1,2,3], Melissa Pelletier[1], Amelie Lachance[1,2,3], Yashar Zeighami[4], Sylvain Iceta[1,5], Laurent Biertho[6], Alain Dagher[7], Andre Carpentier[8], Andre Tchernof[1,2], Andreanne Michaud[1,2,3]

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Subjective valuation (SV) is a key brain process in which value is assigned to options based on perceived benefits. To our knowledge, no study has explored the effects of bariatric surgery on food SV or its associations with appetite-regulating

hormones. We therefore aimed to investigate this, as measured by Willingness-to-Pay (WTP), for both high-caloric density foods (HCF) and low-caloric density foods (LCF). Sixty-one participants with severe obesity, scheduled for bariatric surgery (mean age=43.7±9.3 years; mean BMI=44.2±4.0 kg/m^2) were included. WTP was assessed using the Becker-Degroot-Marschak food auction task during fMRI sessions conducted pre-surgery and at 4, 12, and 24 months post-surgery where participants had to bid between $0 and $5 on HCF or LCF. In each session, blood samples collected during fasted and postprandial states were analyzed for glucagon-like peptide 1 (GLP-1), peptide YY (PYY) and total ghrelin levels. Mixed-effect models showed a significant reduction in mean WTP for HCF post-surgery compared to pre-surgery (pre: $2.38±0.65; 4, 12, 24 months: $1.76±0.88, $p<0.001$; $2.07±0.76, $p<0.001$; $2.17±0.73, $p=0.03$, respectively). No significant changes were observed for LCF ($p>0.05$). WTP for HCF was positively associated with fasted total ghrelin ($\beta=0.002$, $p<0.001$) and negatively with postprandial PYY ($\beta=-0.003$, $p=0.019$). No significant association was found for GLP-1. These findings suggest that bariatric surgery reduces SV specifically for high-calorie foods, which is associated with changes in appetite-regulating hormones. Further fMRI analyses will explore how these variations manifest in brain activity, providing insights into food valuation mechanisms post-surgery.

P126
3:15

Relationship Between Sex Of Parents And Their Child On Clinical Effectiveness Of Family-Based Behavioral Programs

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Family-Based Behavioral Treatment (FBT) effectively treats obesity in parent-child dyads by targeting eating habits, physical activity, and parenting behaviors, yielding better short and long-term weight outcomes than controls. Prior research found greater weight loss in opposite-sex dyads (n=164) over two years. This study builds on those findings with a larger sample, examining differences in the odds of achieving clinically meaningful weight loss. Data from 18 randomized FBT trials with parent-child dyads (children aged 6–12 with overweight/obesity) were analyzed at 6 months (n=822), 1 year (n=750), and 2 years (n=402). Clinically meaningful weight loss was defined as a ≥0.25 zBMI reduction for children and ≥5% body weight loss for parents, both linked to improved health-related outcomes. Logistic regressions tested whether dyad composition predicted success, adjusting for age, baseline height, and weight. Children in opposite-sex dyads were 1.6x, 1.8x, and 1.9x more likely to achieve a 0.25 zBMI reduction at 6 months, 1 year, and 2 years, respectively (ps <0.01). Child sex alone did not predict success. Dyad type did not affect parents' odds of achieving 5% weight loss, but fathers were 2.6x more likely than mothers to reach this goal ($p<0.01$). At 2 years, daughter/mother dyads had the lowest success rates (0.5x for daughters, 0.6x for mothers; ps <0.05), while daughter/father dyads had the highest (3.0x for daughters, 2.1x for fathers; ps <0.05). This trend was consistent at 6 months and 1 year. Parent-child sex dynamics may influence weight loss outcomes in FBT. While speculative, same-sex dyads may share tendencies around eating and activity that reinforce existing habits. Tailoring interventions by dyad composition could enhance treatment effectiveness.

3:30

Multi-Dimensional Architecture-Based Personalized Digital Therapeutic: Development And Initial Clinical Validation For Eating Behavior Intervention In Obese Women

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Background: Obesity is a multifactorial condition influenced by metabolic, behavioral, and psychological factors. Traditional weight loss programs often overlook individual variations in eating behavior, cognitive distortions, and real-time metabolic responses. This study integrates three key components: (1) eating behavior-based tailored interventions addressing emotional eating, external eating, and food addiction, (2) cognitive behavioral therapy (CBT) targeting cognitive distortions prevalent in young women with obesity, such as perfectionism and impulsivity, and (3) continuous glucose monitoring (CGM)-guided personalized dietary management. Methods: A prospective, non-blinded randomized controlled trial was conducted with 105 overweight female participants (BMI ≥23). Participants were classified based on eating behavior tendencies and randomly assigned to an intervention group (n=70) receiving CGM-based personalized coaching with tailored CBT and eating behavior interventions, or a control group (n=35) receiving standard care, including general health education and lifestyle advice, without personalized digital coaching. Outcome measures included body composition, dietary intake, psychological assessments, and buffet test results at baseline, post-intervention, and 8-week follow-ups. Results: Following the digital intervention (DI), significant reductions were observed in emotional eating ($p = .003$), external eating ($p = .041$), and food addiction ($p = .018$) in the intervention group compared to the control group. In the buffet test, the intervention group showed a greater reduction in total carbohydrate intake ($p = .002$) and palatable food consumption in kcal ($p <.001$) compared to the control group, with significant between-group differences. Additionally, the proportion of healthy food choices increased more in the intervention group, with a significant between-group difference ($p = .023$). Regarding body composition, there was a trend toward greater reductions in both body weight and waist circumference in the intervention group ($p <.1$). Conclusion: This study advances the field of digital therapeutics by demonstrating the synergistic effects of CGM, behavioral profiling, and cognitive restructuring in obesity management, offering a scalable, personalized strategy for sustainable weight control.

3:45

Tirzepatide Dampens Food Motivation And Food Cue-Induced Nucleus Accumbens Dopamine ReleaseIn Rats (New Investigator Travel Awardee)

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Recent studies employing the GLP-1/GIP dual analog tirzepatide have shown enhanced weight loss and reduced malaise compared to GLP-1 receptor (GLP-1R) agonism alone. However, the neurobehavioral mechanisms mediating tirzepatide's

superior efficacy over GLP-1 monotherapy are poorly understood. Here, we investigated how tirzepatide influences appetitive motivational processes associated with highly palatable food. In adult male rats, we first confirmed GIPR mRNA expression in the mesolimbic system using fluorescent is situ hybridization. To assess the effect of tirzepatide on motivation for palatable food, rats were trained in an effort-based lever pressing task for high-fat/high-sugar pellets. When tested using a progressive ratio reinforcement schedule, we showed that systemic tirzepatide dose-dependently reduced lever presses and response break point, indicating decreased motivation to work for palatable food. Next, to explore the effects of tirzepatide on food cue-induced nucleus accumbens (ACB) dopamine (DA) signaling, we expressed D2R-based fluorescent sensors in the ACB of rats and measured DA binding during an auditory cue Pavlovian discrimination procedure in which one cue (CS+) signaled liquid sucrose reinforcement, whereas another cue (CS-) did not. Our results revealed that tirzepatide reduced ACB DA binding upon presentation of the CS+ but not the CS-, indicating an attenuation of food cue-associated dopamine release.These results were obtained in the absence of effects on latency to consume sucrose or amount consumed. Collectively, these findings suggest that tirzepatide modulates palatable food motivation by altering mesolimbic DA release, offering new insights underlying the enhanced efficacy of dual GLP-1R/GIPR agonism compared to mono GLP-1R agonism.

4:00 **Semaglutide-Induced Conditioned Taste Aversion Suppresses Dopamine Signaling To Sucrose**

Maxine Loh[1], Cesia Llort[1], Jordan Opoka[1], Mitchell Roitman[1,2]

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Glucagon-like peptide-1 receptor (GLP-1R) agonists (e.g., semaglutide) have been successfully developed to treat diabetes and obesity. However, semaglutide users experience gastrointestinal distress, nausea, and shifts in food preference. Preclinical work shows that GLP-1R agonists can induce a conditioned taste aversion (CTA) – a robust phenomenon where illness associated with initially palatable food promotes subsequent rejection. We have recently shown that phasic dopamine signaling to sucrose is suppressed after acquisition of a lithium chloride (LiCl)-driven CTA. Here, we tested the hypothesis that CTA formed through semaglutide-sucrose pairing will suppress sucrose-evoked phasic dopamine signaling. Dopamine (in vivo fiber photometry) and behavior (DeepLabCut) were recorded during sessions of intraoral 0.3M sucrose delivery. Initially sucrose-naïve rats received injection (i.p.) of either vehicle (Unpaired) or a malaise-inducing dose (10nmol/kg) of semaglutide after the first session (e.g. Conditioning). The following day, rats received the opposite injection in the home cage. This procedure was repeated weekly for 3 pairings. Daily sessions continued without injection (Extinction). While semaglutide caused similar decreases in body weight and temperature in Unpaired and Paired rats, only Paired rats exhibited behavioral evidence of a CTA. Likewise, phasic dopamine responses to sucrose were progressively suppressed with each Conditioning session only in Paired rats. These findings demonstrate that, akin to LiCl, GLP-1 agonism can cause plasticity within the mesolimbic system. Our work provides a platform on which the effects of satiety versus malaise circuits and/or pharmacological interventions against malaise for impact on dopamine signaling can be tested.

4:15 **A Role For Glp-1R Positive Neurons In The Parasubthalamic Nucleus In Appetite Suppression**

Jo Edward Lewis, Danae Nuzzaci, Mireia Montaner, Paula-Peace James-Okoro, Fiona Mary Gribble, Frank Reimann
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GLP-1 receptor (GLP1R) and dual GLP-1/GIP receptor agonists are now widely used to treat diabetes and obesity, however, the physiological importance of different neuronal populations expressing these receptors is still not fully understood. Feeding behaviour is regulated by a network of neuronal populations in the brain and the parasubthalamic nucleus (PSTN), an incompletely understood brain region in the posterior hypothalamus, has been implicated in the regulation of food intake in response to other gut hormones (e.g. CCK and PYY). As mouse models expressing Cre under the control of the GIPR or GLP1R promoter report the PSTN, we sought to investigate the functional importance of these receptors in the PSTN using optogenetic, chemogenetic and viral tracing techniques. Administration of GLP1R or GIPR agonists increased cFOS staining in the PSTN. However, chemogenetic activation of Glp1r-, but not Gipr-expressing PSTN neurons reduced feeding, whilst neither had an effect on intraperitoneal glucose tolerance. We found that PPG (GLP-1 producing) neurons innervate the PSTN, suggesting a role for GLP-1 signalling in this nucleus. Optogenetic activation of PPG fibers in the PSTN also reduced feeding in ad lib fed animals, increasing latency to feeding initiation. Glp1r-expressing PSTN neurons were found to project to distinct brain regions implicated in the control of food intake, including the lateral parabrachial nucleus and the nucleus of the solitary tract. Our studies demonstrate that GLP1R-stimulation in the PSTN is relevant for the control of food intake, likely downstream to PPG neurons in the hindbrain, rather than peripheral GLP-1 signals, which are unlikely to reach this nucleus.

Friday, August 1, 2025

8:00 - 4:30 PM	Registration - South Mezzanine
Registration	

9:00 - 10:00 AM	South Mezzanine
Poster Session 6, Exhibits & Coffee Break	

P401 **Nothing Is Sweeter Than Chocolate: Sugar Preference As A Predictor Of Self-Reported Emotional Eating**

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Emotional eating is defined as the tendency to overeat beyond one's hunger in response to emotions (Macht, 2008). But is emotional eating predicted by emotions solely? We propose an alternative approach in understanding emotional eating by examining a common component in comfort foods: sugar content. A non-clinical population of 60 participants, completed Emotional Appetite Questionnaire (EMAQ, Geliebter & Aversa, 2003), the adapted Monell Forced-Choice task (Mennella et al., 2010) selecting the preferred concentration of sugar in the lab-manufactured chocolate, and rated the level of chocolate liking. They also indicated their favorite commercial chocolate, from which we extracted the amount of sugar it contains. Results showed that chocolate liking and preferred concentration of sugar in lab-manufactured chocolate predicted generalized ($R^2 = .214$, $F(4,55) = 3.73$, $p = .009$) and negative emotional eating scores ($R^2 = .157$, $F(4,55) = 2.55$, $p = .04$), but not positive ones ($R^2 = .101$, $F(4,55) = 1.53$, $p = .20$). Favorite commercial chocolate did not significantly predict emotional eating. To avoid supposed incompleteness in the definition of emotional eating, our findings suggest that a revised alternative perspective should also include non-affective related cues such as food components.

P403 **Impaired Dopamine Transmission In Obese Mice Drives Motor Slowness**

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Physical inactivity, a hallmark of obesity, amplifies the impact of unhealthy eating, worsening health and quality of life. We propose that impaired dopamine transmission in the striatum, a key region for motor control, contributes to difficulties engaging in physical activity. We conducted parallel investigations in humans and mice. In humans, motor engagement was quantified by the latency between trials in a reward-based task in which participants aimed to collect beads. The task was conducted in individuals with normal-weight (n=20) and overweight/obesity (n=23). A similar task, with food-pellets, was then conducted in two sets of mice: a chow-fed group (n=25) and a six-weeks high-fat-diet exposed group (n=18) displaying significant weight gain and impaired glucose tolerance, metabolic signs of obesity. Using an innovative fiber-photometry approach to visualize dopamine transmission, we compared striatal dopamine transmission between the two groups of mice. Analysis was conducted between groups with paired or unpaired t-test (α=0.05). Results indicate that humans with overweight/obesity exhibit a longer latency between trials (2.7s vs. 3.4s), indicating motor slowness. Similarly, HFD-fed mice displayed a higher latency to retrieve the pellet (0.8s vs. 1.5s) and a significant reduction of dopamine transients in the striatum 4.7/min vs. 3.6/min). While the underlying mechanisms linking obesity to reductions in dopamine release remain to be understood, the correlation between glycemia and motor slowness in mice indicates possible roles for hyperinsulinemia or hyperglycemia modulating in dopamine transmission. Future studies will aim to clarify this link between hyperinsulinemia and the impaired dopaminergic transmission.

P405 **Validating Ocosense Glasses In Home-Based Studies: Assessing Usability And Performance.**

Martin R Yeomans[1], Aishwarya Padmanabhan[1], Sophia Cox[1], Tatum Sevenoaks[1], Rhiannon M Armitage[1], Simon Stanoski[2], Filip Panchevski[2], Borjan Sazdov[2], Mia Darkovska[2], Claire Baert[2], Mohsen Fatoorechi[2], Hristijan Gjoreski[2], Charles Nduka[2]
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Measuring eating behaviour in the real world relies on self-report, and is prone to underreporting and subjectivity. The OCOsense glasses offer a promising alternative by directly monitoring facial muscle movements to automatically detect chewing behaviour, overcoming these limitations. Findings from a lab-based study where we analysed chewing data from the intake of breakfast foods indicate that the OCOsense glasses accurately detect overall facial movement to identify 81% eating and 85% non-eating events. Expanding on this, we conducted a two-week home-based study to test these glasses in a real-life setting. Twelve participants, aged 18-45 (67% female), were equipped with the OCOsense glasses and a corresponding mobile application. Eating event data (i.e., when the glasses detect active chewing) were recorded using the glasses for two weeks, with participants annotating and photographing meals while wearing the glasses in week two. Based on participant feedback, in which they received a notification to confirm or deny each detected eating activity, the real-time eating detection algorithm on the smartphone accurately identified 86% of eating events. Additionally, an AI food identification algorithm was implemented to identify the food items and nutritional information using the images captured by participants with the glasses camera. Participants rated the AI model's accuracy in food detection at an average of 8.5 out of 10. This suggests a strong user-perceived accuracy and effectiveness of the glasses algorithm, highlighting the capability of smart eyewear technology to detect eating events and monitor food intake in real-life settings.

P407 **The Effects Of Stevia On Acute Endocrine Hormone Release In Men And Women With Normal Weight, Overweight And Type 2 Diabetes**

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Stevia is a plant-based, zero calorie sweetener, and its effects on the human endocrine system are not well studied. This investigation evaluated the effects of beverages sweetened with stevia, glucose, a combination of glucose + stevia, or water on acute glycemic and appetite regulatory hormone responses. We hypothesized that stevia would have no material effects on acute endocrine responses. In a randomized, double blind, crossover study, healthy individuals (n=23 per group) with normal weight, overweight, or type 2 diabetes mellitus consumed 473 ml beverages containing either 25% of the acceptable daily intake of stevia (75.6 mg steviol equivalents, 0 kcal), 30 g glucose (120 kcal), 30 g glucose + stevia (120 kcal), or water (0 kcal). Blood samples were collected at 30 to 60 min intervals over 180 min and analyzed for glucose, insulin, glucagon, glucagon-like peptide-1 (GLP-1), peptide YY (PYY), and glucose-dependent insulinotropic polypeptide (GIP) concentrations. For individuals with overweight, the incremental area under the curve (iAUC) for plasma concentrations of glucose increased significantly more with glucose [median: 1779 min*mg/dL)] and stevia + glucose [median: 1988; min*mg/dL] compared to the stevia [median 47.4 min*mg/dL] and water [18.9 min*mg/dL] beverages (P<0.001). Similarly, the iAUC for insulin increased significantly more with the glucose [1017 min*mU/L] and stevia + glucose [1155 min*mU/L] beverages compared to the stevia [56.3 min*mU/L] and water [12.8 min*mU/L] beverages (P<0.001). The iAUC for GIP increased significantly more with the glucose [4583 min*pg/mL] and stevia + glucose [7133 min*pg/mL] beverages compared to the stevia [72.4min*pg/mL] and water [1.25min*pg/mL) beverages (P<0.001). There were no differences between beverages for glucagon, PYY, GLP-1. Data from individuals with normal weight and type 2 diabetes mellitus are undergoing analysis. The stevia beverage had no clinically important effects on acute appetite regulatory hormone responses or subsequent energy intake in individuals with overweight. The acute hormone responses to stevia + glucose was similar to those for glucose alone.

P409 **A Novel Mouse Model Of Mild Chronic Social Stress Elicits Anxiety-Like Behaviours And Hyperphagia Of Palatable Liquid Diet.**

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Chronic stress is associated with obesity and exacerbated binge-eating. In particular, mild chronic stress is associated with palatable food intake in humans. However, the underlying neural circuits are poorly understood, partly due to the lack of valid rodent models. Here, we refined a novel mouse model of mild chronic social stress (mCSS) and assessed its ability to induce hyperphagia of palatable diet. C57BL/6J mice were moved daily to new cages and briefly exposed to a resident male, ex-breeder CD1 mouse. Upon any sign of aggression, the mice were separated by a perforated wall. Each day, mice were exposed to a new CD1 mouse for up to 14 days. Controls were weighed each day but otherwise left undisturbed. As expected, when given access to chow only, mCSS mice (n=6) gained -3.4%points less body weight than controls (n=6) after 7 days of mCSS(95%CI:-6.1, -0.7; p=0.017; unpaired t-test). In a social avoidance test, mCSS mice (n=6) did not interact significantly more with a novel CD1 mouse than an empty enclosure, while control mice (n=6) did (control: p=0.016,mCSS: p=0.8;Šidák's multiple comparisons). Additionally, mCSS mice (n=8) increased the percentage of time they spent immobile in the open field by 7.5%points compared to controls (n=8) (95%CI: 3.1, 11.9; p=0.003; unpaired t-test). In a new cohort of mice, intermittent access to Ensure chocolate milkshake was provided to both control (n=8) and mCSS mice (n=8) every 3 days for 3h throughout the mCSS paradigm. On the final day,mCSS mice consumed 0.2g more milkshake over 2h than controls (95%CI:0.07, 0.3;P=0.012; unpaired t-test). Overall, the mCSS paradigm induces anxiety-like behaviours and palatable diet hyperphagia; presenting a novel paradigm to study how stress contributes to binge-like eating and obesity.

P411 **Central Mechanisms Of Glucose-Dependent Insulinotropic Polypeptide (Gip)-Mediated Appetite Regulation**

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Institute of Metabolic Science - Metabolic Research Laboratories & MRC-Metabolic Diseases Unit, University of Cambridge, Cambridge, United Kingdom

GIP and glucagon-like peptide-1 (GLP-1) regulate insulin secretion and appetite. Combinatorial obesity therapies targeting both the GIP and GLP-1 receptor demonstrate superior glycemia- and weight-lowering effects compared to GLP1R agonists alone. However, the role of GIP in appetite regulation and its mechanism of action remains unclear. This study aimed to identify the central areas through which GIP modulates food intake and further explore the physiological functions of endogenous GIP.

Using transgenic *Gip*-Cre x Rosa26-hMD3Dq mice (Gip^{Dq}) to stimulate intestinal GIP-secretion, or intraperitoneal D-Ala2-GIP injection, we observed significant suppression of food intake and increased neuronal activity (via c-Fos staining) in the hypothalamus and brainstem—key feeding centers of the brain. Co-localization of c-Fos and GFP in mice labelling *Gipr*-expressing cells Cre-dependently ($Gipr^{eGFP}$) showed stronger overlap in the brainstem than in the hypothalamus, suggesting brainstem GIPR neurons as primary targets. Intraduodenal glucose infusion increased c-Fos expression in hypothalamic and brainstem $Gipr^{eGFP}$ neurons by ~200% versus saline, indicating that GIPR neurons respond to peripheral food-related cues. Additionally, stimulating intestinal K cells in Gip^{Dq} mice blocked peptide YY (PYY)-induced avoidance responses, suggesting that GIP's anti-emetic effects are mediated by endogenous mechanisms rather than purely pharmacological actions (n = 6–10/group, One-way ANOVA).

Our findings highlight that GIP's appetite-suppressing effects are mediated by central GIPR signalling, particularly in the brainstem. Understanding these mechanisms provides insights that may guide the development of improved incretin-based therapies for obesity and type 2 diabetes.

P413 **Towards Fine-Scale Targeting Of Neural Substrates Controlling Feeding And Autonomic Function: Novel Meso- And Microscale 2-D And 3-D Organization Of Rat Catecholaminergic And Neuropeptidergic Circuits In The Hindbrain And Hypothalamus**

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The intracranial targeting of cell types controlling feeding and regulating autonomic function has been facilitated by stereotaxic brain atlases, but the fine-scale organization of axonal systems in wild-type animals is poorly known. This makes more specific targeting of axonal terminal fields difficult, especially in rats, for which fewer transgenic lines exist and for which, consequently, genetic manipulation must rely heavily on intracranial injection of retrogradely-directed viral vectors along precise coordinates. Here, we report new organization of key feeding and autonomic control regions in the rat forebrain and hindbrain, charting the cell bodies and axons for over a dozen of their neurotransmitter and neuropeptide systems, specifically in prefrontal cortex, septum, hypothalamus, parabrachial nucleus, ventrolateral medulla, and dorsal vagal complex (N=4–7 per system). The data are organized as open-access, interactive, and downloadable atlas maps, complete with stereotaxic coordinates. These include, for the first time, “heat maps” providing spatial averages of axonal patterns from multiple rats, allowing one to better understand previously hidden intersubject variation, thereby refining the list of coordinates that will likely produce the most accurate targeting. We also report novel 3-D organization of rat hindbrain catecholaminergic systems, including a structural basis for interhemispheric coordination. Collectively, this new, fine-scale organization of feeding and autonomic control circuits provides critical spatial information to aid in their targeting and for deeper hypothesis-driven interrogation of these systems to understand motivation, reward, and autonomic control in the rat model organism.

P415 **Controlling Food Intake: The Role Of Prefrontal Cortical Projections To The Nucleus Accumbens And The Basolateral Amygdala**

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Background: Stressful events can drive towards impulsive actions and increased consumption of palatable foods. The prefrontal cortex (PFC) plays a critical role in regulating these behaviors, yet how stress influences PFC’s encoding of food intake remains unclear. Dopamine, which is released into the PFC during stress, can be a potential trigger for stress-induced changes. Notably, dopamine-sensitive PFC neurons project to various brain regions, including the basolateral amygdala (BLA) and the nucleus accumbens (NAc). We hypothesize that these distinct PFC projections play differential roles in stress-induced overeating and impulsivity. **Experimental design**: Using viral vectors, we enabled pathway-specific chemogenetic manipulation and photometric recordings in male C57BL/6 mice. Palatable food intake was measured by consumption of high-fat food, while impulsive behaviors were assessed using the 5-choice serial reaction time task. Stress was induced through social defeat or yohimbine administration. **Results**: Photometric recordings of dopamine dynamics in the PFC revealed increased dopamine release in response to both rewarding stimuli (e.g., fat intake) and stressful experiences (e.g., social defeat or foot shock). Chemogenetic activation of dopamine-sensitive PFC–BLA projections increased fat intake, while initial results suggest that stress-induced impulsivity remained unaffected. In contrast, activation of PFC–NAc projections reduced impulsive actions induced by stress, without affecting food intake **Conclusions**: Our findings demonstrate that distinct PFC projections to the NAc and BLA differentially modulate stress-induced overeating and impulsivity. These results contribute to the development of targeted interventions for stress-related disorders.

P417 **Hindbrain Ramp2 Mediates Cagrilintide&Rsquo;S Anorectic Effects**

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Cagrilintide, a long-acting amylin analogue, is in clinical development for the treatment of obesity and type-2-diabetes. Cagrilintide binds to both calcitonin receptors (CalcR) and amylin receptors, which are composed of the CalcR associated to a receptor modifing protein (RAMP1, 2, 3), resulting in three subtypes of the amylin receptor (AMYR1, 2, 3). The brain feeding circuits targeted by this drug remain poorly understood. To first identify key metabolic brain regions activated by cagrilintide, CalcR-cre-tdTomato mice (n=8/group) were injected with cagrilintide (10 nmol/kg, i.p.) after a 12-hour fast. Cagrilintide increased cFos expression in CalcR+ neurons of the area postrema and nucleus tractus solitarius (NTS), among other regions. Given that these regions are rich in RAMPs, which mainly colocalize with CalcR, we investigated if specific amylin receptor subtypes contribute to the effects of amylin and cagrilintide. Previous studies had shown that AMYR1 and AMYR3 mediate amylin’s effects on glucose control and food intake, respectively, as well as cagrilintide’s effects on body weight, but the role of RAMP2 remains unexplored. To address this gap, RAMP2-flox mice were injected with an AAV-Cre vector (n=9) into the NTS to selectively and site-specifically knock out the *Ramp2* gene. Upon cagrilintide injections, control-virus-treated mice (n=5) exhibited reduced food intake at 12h, whereas no difference was observed in RAMP2-KO mice as compared to vehicle-injected mice. Despite similar cFos activation in both groups of mice, our findings suggest that DVC^{RAMP2} is necessary for cagrilintide’s anorectic effect. Our studies provide new insights into cagrilintide’s neural mechanisms, highlighting the hindbrain as a key region, and the AMYR2 specific role.

P419 **Regulation Of Asprosin In The Acuate Nucleus Of The Hypothalamus By Nutritional State.**

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Asprosin is a fasting-induced adipokine that crosses the blood-brain barrier and activates orexigenic agouti-related peptide (AgRP) neurons in the arcuate nucleus (ARC) of the hypothalamus, suggesting a role in appetite regulation. While fasting increases asprosin in the periphery and cerebrospinal fluid, it is unclear whether ARC asprosin expression changes in response to fasting. To test this, we assigned adult male and female Long Evans rats (n = 24; 6 per sex per condition) to either a sated or overnight fasted condition. Brains were collected and processed for immunohistochemical detection of asprosin in the ARC. Asprosin expression was quantified as the percentage of the total image area covered by asprosin-positive staining using image thresholding and automated analysis. We hypothesized that overnight fasting would increase asprosin levels in the ARC. A 2 x 2 ANOVA (sex x condition) revealed no significant main effects or interactions. However, preliminary findings suggest a potential increase in ARC asprosin expression in fasted animals compared to sated controls. To confirm this finding and expand on whether fasting reliably induces a peripheral increase in asprosin, ongoing work in our lab is expanding the sample size and measuring circulating plasma asprosin levels. Together, these data will provide insights into the mechanisms by which energy state modulates hypothalamic circuits involved in appetite and metabolism.

P421 **A New View On The Central Response Of Semaglutide By Functional Ultrasound In Mice**

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Semaglutide, a GLP-1 receptor agonist, has revolutionized obesity therapy by delivering unprecedented weight loss and metabolic benefits. It also shows promise for neurological conditions by improving craving and addictive behaviors, cognitive function, and symptoms of neurodegenerative disorders like Alzheimer's and Parkinson's diseases.
We examined semaglutide's effects on the mouse brain network using functional ultrasound imaging. Animals were mildly anesthetized before receiving 20 nmol/kg semaglutide. Following baseline recording, we monitored cerebral blood volume (CBV) and functional connectivity (FC) changes for 75 minutes. We used the mouse brain reference atlas (Allen Institute for Brain Science) to map brain regions. For preprocessing and analyses, we used a workflow based on the SPM12 software package. Semaglutide decreased CBV in the hypothalamus, septum, amygdala, ventral tegmental area (VTA), nucleus accumbens, and hippocampus. FC analyses revealed increased amygdala and cortical FC within 20-30 minutes post-injection, maintained throughout the experiment. Later scans showed decreased FC in the olfactory cortex, nucleus accumbens, VTA, and substantia nigra.
Our data indicate early activation of aversion networks in the amygdala and prelimbic cortex, along with reduced CBV and FC in the mesolimbic pathway. Pronounced CBV changes in the hypothalamus and septum shed light on the circuitry underlying semaglutide's central effects. Further investigations will explore brain wide CBV changes related to dose response and treatment duration, potentially leading to new neuropsychiatric therapies.

P423 **Weight Regulation By Glp1R Agonists Via A Non-Canonical Hypothalamic Pka-Mtorc1 Mediated Pathway**

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Glucagon-like Peptide-1 Receptor agonists (GLP1Ra) promote weight loss, yet the molecular mechanism behind this effect is unknown. We show that GLP1Ra increase PKA-mediated phosphorylation of the mechanistic Target of Rapamycin Complex-1 (mTORC1) subunit Raptor at Ser^{791} and whole-body mutation of Ser^{791} to Ala (S791A) in Raptor attenuates the anorectic effect of GLP1Ra. These results fail to demonstrate the cell type where PKA-mediated Raptor phosphorylation contributes to the anorectic effect of GLP1Ra. We hypothesize that proopiomelanocortin (POMC) neurons contribute to the anorectic effect of GLP1Ra via PKA phosphorylation of mTORC1. We tested our hypothesis by developing two tamoxifen-inducible Cre-driven mouse lines that either knock down (KD) Raptor in POMC neurons (iPOMC-Raptor KD) or that knock in S791A in Raptor in POMC neurons (iPOMC-Raptor KI). Cre induction in both mouse lines also labels POMC neurons with tdTomato with an ~84% efficiency. We observed a ~45% KD of Raptor in iPOMC-Raptor KD vs. control mice in $tdTomato^{+}$ cells and no difference in Raptor expression between iPOMC-Raptor KD and control mice in $tdTomato^{-}$ cells (n=3-4/group). To test whether Raptor and S791A in Raptor in POMC neurons contribute to the anorectic effects of GLP1Ras, iPOMC-Raptor KD and iPOMC-Raptor KI mice were fed a 60% high fat diet (HFD) and weights were measured during a 14-day GLP1Ra treatment period. There was no difference in GLP1Ra-induced weight loss between control and iPOMC-Raptor KD and a trend for iPOMC-Raptor KI mice to be less sensitive to the anorectic effects of GLP1Ra (n=7-9/group) in both male and female mice. Although preliminary, our results suggest that the Raptor Ser^{791} residue in POMC neurons partially contributes to the anorectic effect of GLP1Ra.

P425 **Cortical Control Of The Lateral Hypothalamus**

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The lateral hypothalamus (LH) is a critical controller of ingestive behaviours and metabolism. Due to its lack of strong local synaptic connectivity [10.1016/j.cub.2020.07.061 ; 10.1016/j.cub.2022.05.029], long-range synaptic input is poised to decisively control the output of LH neurons. In this bottom-up project we characterized the role of glutamatergic inputs from the neocortex to the LH. We anatomically analysed cortical source regions using retrograde tracing. With optogenetic circuit mapping, we show that the medial prefrontal cortex (mPFC) is the strongest cortical input to the LH. The mPFC particularly

strongly excites LH neurons with low responses to the hunger hormone ghrelin, and inhibitory responses to the satiety hormone leptin. Therefore, the mPFC opposes natural satiety signals in the LH, and does not interfere with hunger signalling. To test the role of this pathway in vivo, we used designer receptors exclusively activated by designer drugs (hM4Di) to inhibit mPFC output to LH. We used a 24/7 behavioural monitoring strategy in a custom-built foraging maze [10.24072/pcjournal.416], and found that blocking mPFC output to LH decreased the length of feeding bouts. Together, these results suggest that the direct, monosynaptic pathway from mPFC to LH acts to oppose satiety.

P427 **Sweet Paradox: Investigating Links Between Glp-1 In The Taste System And Sugar Intake**

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Glucagon-like peptide 1 (Glp1) agonists have proven effective for weight loss in part through appetite suppression. Glp1 and its receptor (Glp1r) are expressed in the peripheral taste system, predominately in sweet taste cells and nerve terminals respectively, and Glp1r is highly expressed in central reward areas. Here, we investigated links between Glp1, the taste-reward axis, and the hedonic appeal of sugar. Using an shRNA-based virogenetic approach, we found that loss of Glp1r in the major taste fields attenuated the initial lick avidity for glucose, particularly at perithreshold concentrations, in rats. Next, we tested if Glp1r in the taste papillae is associated with sweet receptor expression. We found that sweet receptor knockout mice had less Glp1r mRNA than sweet-sensitive C57BL6/J (B6) mice, and within the sweet-sensitive mice, Glp1r was positively correlated with the expression of a sweet receptor gene, Tas1r3, and a downstream transduction intermediary, Trpm5. We additionally explored if chronic treatment with semaglutide (SEMA; Glp1r agonist) affected 5% sucrose intake and associated signaling mechanisms along the taste-reward systems of B6 mice. We observed that 5-10 nmol/kg SEMA led to a reduction in body mass over 10 days of treatment. However, sucrose intake increased after SEMA treatment. This effect was not due to caloric deficit or lowered blood glucose levels. Glp1r expression was upregulated in the taste papillae, while, centrally, Glp1r and dopamine 1 receptor expression were downregulated in the dorsal striatum of the SEMA-treated mice. Thus, contrary to expected effects on appetite, it appears that Glp1-related signaling along the taste-reward axis may contribute to increased sugar consumption under certain conditions.

P429 **From The Pancreas To The Dorsal Raphe &Ndash; A Novel Neural Substrate For Amylin&Rsquo;S Effects On Ingestive And Motivated Behavior.**

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The gut-brain axis has been successfully exploited to create potent pharmacotherapies to control appetite. The pancreas also plays a significant role in metabolism, but the pancreas-brain axis is underexplored for weight management. Historically, the pancreatic hormone amylin's effect on food intake was thought to be mediated primarily by amylin receptors in the area postrema (AP). However, there has been a growing body of evidence for amylin acting on areas outside the AP. Notably, high levels of amylin binding have been detected in the dorsal raphe (DR), the main source of serotonin for the forebrain. Here, we aim to investigate the DR as a new target for amylin's effect on feeding-related behaviors. To examine the sufficiency of amylin to control ingestive and motivated behaviors, food intake, motivation, preference, and meal patterns were measured in Sprague-Dawley rats (10-13, each sex) following acute intra-DR injections of amylin. Pharmacological stimulation of DR amylin receptors led to profound decreases in food intake and changes in meal patterns in both sexes. Moreover, it reduced food-seeking and food-motivated behaviors for sucrose pellets, effect which was more robust in females. To determine the necessity of amylin signaling in the DR for metabolic control, a virogenetic knockdown of the core amylin receptor component, CTR, in the DR was used (12-13, per sex & treatment). Loss of amylin signaling in the DR led to an increased preference for highly palatable foods, primarily fat-driven in males. Thus, we identified the DR as a novel neural substrate for amylin's actions on ingestive and motivated behavior. These results have potential translational relevance, as amylin-based pharmacotherapy is under investigation as a potential anti-obesity therapeutic.

P431 **Mesolimbic Amylin Receptor Activation Suppresses Motivation For Palatable Fluids In Female Rats**

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The pancreatic peptide amylin promotes negative energy balance through actions in the brain, and is considered a promising target for obesity treatment. Prior work has shown that activation of amylin receptors (AmyR) in the ventral tegmental area (VTA) with the agonist salmon calcitonin (sCT) suppresses palatable food intake, and particularly fat intake, in male rats. However, less is known about how mesolimbic amylin signaling impacts feeding behaviors in females, and whether this might be impacted by estrogen. Here, we tested the hypothesis that intra-VTA sCT would decrease operant responding for isocaloric fat or sucrose solution in female rats, and tested this in both ovariectomized and intact animals to evaluate whether chronic levels of ovarian hormones like estrogen might influence responses. Results indicated that VTA AmyR activation significantly suppressed progressive ratio responding for each solution ($p<0.05$), but ovarian status did not alter these responses ($p>0.05$). To assess whether motor effects of sCT might underlie reduced lever pressing for fat/sucrose, in a separate group of female rats, we tested locomotor activity in an open field apparatus after VTA sCT injection. No significant effects of VTA sCT were detected for the distance traveled in the 2h after sCT administration ($p>0.05$), suggesting that VTA AmyR activation does not produce potent locomotor deficits. Together, these findings contribute to an emerging literature demonstrating the ability of VTA AmyR signaling to promote negative energy balance in female rats, but suggest that chronic estrogen does not influence the impact of VTA sCT on motivated behavior for palatable macronutrient solutions.

P433 **Metformin Use In Murine Obese Pregnancy Disrupts Offspring Hypothalamic Neural Progenitor Cell Proliferation**

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C Pantaleao, Susan E Ozanne, Laura Dearden
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Metformin is widely used in gestational diabetes to regulate maternal glycemia and reduce fetal macrosomia. However, recent human studies have shown that in utero metformin exposure may be associated with increased adiposity in children after birth. The cause of this increased adiposity is unknown, but as metformin freely crosses the placenta, there may be a direct action of metformin on fetal neurodevelopment. We hypothesize that metformin enters the fetal brain and disrupts early hypothalamic development by impairing neural progenitor cell (NPC) proliferation. Obese, diabetic C57b/6J female mice were dosed with metformin during pregnancy and fetal brain tissues were collected on embryonic day 13. We used an embryonic hypothalamic cell line (mHypoE-N46) and fetal hypothalamic neurosphere cultures to examine metformin's impact on NPC proliferation in vitro.Using LC-MS we measured metformin levels in the fetal brain. Metformin transporter expression in the fetal brain was measured by qPCR. A RESIPHER system was used to measure oxygen consumption rate, and immunofluorescence staining was used to assess proliferation after metformin administration in vitro. The metformin transporter PMAT is expressed in the fetal brain. Metformin is detectable in the fetal brain after administration to the mother during pregnancy. In vitro, metformin induced a dose-dependent decrease in oxygen consumption and shift toward glycolysis. This was accompanied by reduced proliferation of NPCs. Our findings indicate that metformin exposure during gestation could interfere with early hypothalamic development, predisposing offspring to energy homeostatic dysregulation and later obesity.

P435 **Determinants Of Body Weight Gain In New Zealand Obese (Nzo) Mice: The Role Of Initial Body Composition And Time-Dependent Variables**

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Obesity is often attributed to a sustained increase in food intake (FI) and/or reduced total energy expenditure (TEE); but the relationship between additional dynamic variables including body weight (BW) and adiposity index (AI=fat/lean mass), that influence energy balance needs refinement to determine the best prediction model for BW gain. We aimed to determine which of these variables better predicted BW gain in mice. For 12 weeks, female NZO/HlLtJ mice (n=23) were fed a high carbohydrate diet, and AI, BW, TEE and FI were measured longitudinally. The hypothesis was that decreased TEE is the best predictor of BW gain. We evaluated four groups of models to identify the best predictors of BW gain using: (1) all **B**aseline AI and FI **V**alues (**BV**), (2) the **R**ate **O**f **C**hange for all these **V**ariables (**ROCV**), (3) either baseline or rate of change values for **S**ingle **V**ariables (**SV**) and (4) **all** baseline and rate of change values (**FULL**). To determine the model with the best predictive power, a repeated k-fold cross-validation (folds=5, repeats=100) method was used and the root mean square error (RMSE) was reported, while accounting for model complexity using the Akaike information criterion (AIC) and likelihood ratio test (LRT). Contrary to our hypothesis, the model including the TEE did not perform better than the null model ($p=0.837$, LRT, $AIC_{TEE}=69.33$, $AIC_{null}=68.24$). The **ROCV** model showed the best fit (RMSE=0.42), followed by **FULL** (RMSE=0.54), and performed better than the null model ($p<.001$, LRT, $AIC_{ROCV}=20.82$). Also, baseline AI showed higher predictive power than TEE (RMSE=0.58, $AIC_{AI}=41.76$). These results suggest that studies of obesity progression should apply an approach rooted in interindividual variation and dynamic change, rather than focusing solely on FI or TEE.

P437 **A Colon-To-Vagus Circuit For Microbial Patterns Regulates Feeding**

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Like their mammalian host, gut microbes require nutrients. However, microbes rely on the host to feed them. How the host senses and responds in real-time to stimuli arising from resident microbes remains largely unknown. Here, we show that in the mouse colon, the microbial pattern protein flagellin stimulates Toll-like receptor 5 (TLR5) expressed on peptide YY (PYY)-labeled colonic neuropod cells. This stimulation of TLR5 by flagellin leads to a reduction of food intake for one-hour (n= 5; $p<0.05$ by ANOVA). Likewise, mice lacking TLR5 in PYY cells (n=9) gain weight at a faster rate than controls (n=6; $p<0.05$ by rmANOVA), and have increased meal size ($p<0.05$ by two-way ANOVA). Because PYY cells contact sensory nerve fibers (21.7±0.6%, N=50 cells), we asked whether flagellin in the colon increases vagal firing rate. Using electrophysiology of the vagus nerve, we found significantly elevated firing rate of the vagus nerve when following a colonic flagellin infusion (n=7, $p<0.05$ by two-way ANOVA). Critically, this vagal response to flagellin is absent when PYY colon cells are optically silenced (n=4) and when TLR5 is conditionally deleted from PYY cells (n=4; $p<0.05$ by Kruskal Wallis test). We found that flagellin is transduced from the colon to the vagus nerve by PYY release. Colon epithelia bathed in flagellin release PYY (n=4, $p<0.05$ compared to buffer by ANOVA). Pharmacologically blocking the PYY receptor NPY2 attenuated the food intake-suppressive effects of flagellin (n=10, $p<0.05$ by rmANOVA). The sensory modality described here enables a host to adjust its behavior by detecting molecular patterns from its resident microbes.

P439 **Assessing The Influence Of Social Isolation On Type 2 Diabetes In Middle-Aged Rats**

Jassmyn J. Venegas, Ziyu Zhang, Chan Young Choi, Milan F. Monroe, Advaita S. Jain, Thyia IIankovan, Yun-Sheng Chen, Nu-Chu Liang
University of Illinois Urbana-Champaign, Champaign, IL, United States

Type 2 diabetes mellitus (T2DM) typically develops in individuals aged 45 and older. Most rodent models, however, use young adults. In humans, social isolation is associated with an increased risk of T2DM. Accordingly, we aimed to establish T2DM and investigate the impact of social isolation in middle-aged rats. The experiment included three housing conditions: pair-housed (CTL, n = 6/sex), groups of 4 per cage (GH, n = 8/sex), or individually housed (ISO, n = 6/sex). CTL rats received a vehicle injection and a control diet. T2DM in GH and ISO rats was induced by alternate feeding of a high-fat and a high-fructose diet (HFFD) combined with a streptozotocin injection (STZ, 30 mg/kg, i.p.). Non-fasting blood glucose (non-FBG) and FBG were measured four times throughout the study. FBG >150 mg/dL and non-FBG >200 mg/dL indicate diabetes, but distinguishing T1DM from T2DM requires assessing insulin sensitivity. Thus, all rats underwent oral glucose tolerance (OGTT) and insulin tolerance (ITT) tests at the end of a 12-week period. The results showed that FBG is not sensitive for detecting diabetes in rats. Regardless of housing condition, significantly more male than female STZ-injected rats met the non-FBG criterion for diabetes. Compared to females, male rats had higher insulin resistance as evaluated using

HOMA-IR and $ISI_{0,120}$ calculated via BG and insulin levels measured from FBG and OGTT. Notably, the severity of diabetes worsened in males but improved in females as the HFFD continued. Finally, the effect of social isolation on T2DM was inconclusive due to the small sample size as well as the complexity in distinguishing T1DM and T2DM. These results warrant further studies to determine the influence of social isolation on the development and prognosis of DM.

10:00 - 11:30 AM	L2

Symposium 5: The Competition is On! Balancing ingestive and competing behaviors

(Celebrating the 75th Anniversary of NIDDK)

Chair(s): Andrew Lutas

10:00 **Simple Pleasures: Regulation Of Feeding And Social Interactions By The Lateral Hypothalamus**

Anne Petzold, Rebecca Figge, Hanna van den Munkhof, Tatiana Korotkova
University of Cologne, Cologne, Germany

Animals have to coordinate and prioritize multiple, at times competing basic needs to ensure survival and reproduction. Nutritional needs, such as hunger and thirst, ought to be balanced and weighed against competing needs like mating. Despite a long-known crucial role of the lateral hypothalamus (LH) in the regulation of hunger and thirst, the neuronal mechanisms enabling representation and orchestration of multiple innate behaviours are not yet understood.Using deep-brain calciumimaging in freely behaving mice, optogenetics and chemogenetics, we investigated functions of two complementary neuronal populations in LH in feeding and social interaction. Despite hunger or thirst, leptin receptor-expressing LH neurons limit feeding and drinking while promoting social interaction, and encode conspecifics of opposite sex. Conversely, neurotensin-expressing LH neurons specifically prioritize drinking despite hunger, and reduce social interactions. Thus, both LH populations act in a complementary manner to enable the flexible fulfillment of multiple essential needs.

10:30 **Threat Modulation Of Appetite: Hypothalamic Neuronal Mechanisms At Play**

CELINE RIERA
Cedars-Sinai Medical Center

Despite extensive knowledge about integration of hormonal cues in the mediobasal hypothalamus (MBH) to control feeding and energy expenditure processes, the impact of sensory cues in this brain area has remained poorly understood. We have showed that cholecystokinin expressing neurons in the dorsomedial hypothalamus integrate olfactory cues associated with predator threats. We present new results characterizing the functional output of these neurons on feeding in health and obesity.

11:00 **A Hypothalamic Circuit That Modulates Feeding And Parenting Behaviors**

Michael J Krashes[1], Ivan C Alcantara[1,2]
[1]NIDDK/NIH, Bethesda, MD, United States, [2]Brown University, Providence, RI, United States

Across mammalian species, new mothers undergo behavioral changes to nurture their offspring and meet the caloric demands of milk production. While many neural circuits underlying feeding and parenting behaviors are well characterized, it is unclear how these different circuits interact and adapt during lactation. Here, we characterized the transcriptomic changes in the arcuate nucleus (ARC) and the medial preoptic area (MPOA) of the mouse hypothalamus in response to lactation and hunger. Furthermore, we showed that heightened appetite in lactating mice was accompanied by increased activity of hunger-promoting agouti-related peptide (AgRP) neurons in the ARC. To assess the strength of hunger versus maternal drives, we designed a conflict assay where female mice chose between a food source or a chamber containing pups and nesting material. Although food-deprived lactating mothers prioritized parenting over feeding, hunger reduced the duration and disrupted the sequences of parenting behaviors in both lactating and virgin females. We discovered that ARC^{AgRP}neurons inhibit bombesin receptor subtype-3 (BRS3) neurons in the MPOA, a population that becomes more active postpartum and governs parenting and satiety. Selective activation of this ARC^{AgRP} to $MPOA^{BRS3}$circuit shifted behaviors from parenting to food-seeking. Thus, hypothalamic networks are modulated by physiological states and work antagonistically during the prioritization of competing motivated behaviors.

10:00 - 11:30 AM	L1

Oral Session 7: Beyond Homeostasis; how reward and learning influence eating

Chair(s): Vaibhav Konanur

10:00 **Hypothalamic Circuits Shape Accumbal Dopamine Release To Drive Feeding (Elsevier Physiology & Behavior New Investigator Travel Awardee)**

Sam Z. Bacharach[1], Laryssa O. Coutinho[1], Katie A. Zappetti[1,2], Amber L. Alhadeff[1,2]
[1]Monell Chemical Senses Center, Philadelphia, PA, United States, [2]University of Pennsylvania, Philadelphia, PA, United States

Agouti-related protein (AgRP)-expressing neurons in the Arcuate nucleus of the hypothalamus (Arc) are tuned to hunger state and critical for feeding behavior. Stimulation of AgRP neurons robustly drives food intake and increases nucleus accumbens (NAc) dopamine (DA) release to food. However, the neural mechanisms linking energy-sensing circuits to mesolimbic DA remain poorly understood. Here, we combined chemogenetic manipulations with *in-vivo* fiber photometry measurements of a DA sensor in mice (n=79) to test the hypothesis that AgRP neurons bidirectionally modulate DA release to food. We used ANOVA with post hoc t-tests to analyze data. Chemogenetic excitation of AgRP neurons increased NAc DA release to food presentation; conversely, inhibiting AgRP neurons under mild food restriction attenuated DA responses to food. DA release positively correlated with subsequent food intake, and pharmacological blockade of NAc DA receptors suppressed AgRP neuron-driven feeding. Further, these effects depended on olfaction, suggesting AgRP neurons drive food-seeking by enhancing DA responses to food-related olfactory cues. We next probed circuit mechanisms mediating this effect by optogenetically stimulating seven major Arc^{AgRP} projections while recording NAc DA (n=75 mice). Stimulation of Arc^{AgRP} projections to the BNST, LHA, PVH, or PVT, but not the CeA, PBN, or PAG, robustly increased food

consumption, confirming previous reports. Stimulation of Arc^{AgRP} projections to the LHA, PVH, and PVT increased NAc DA when food was present, but not from axon stimulation alone. Ongoing studies investigate downstream neuronal populations linking Arc^{AgRP} neurons to NAc DA release. These findings support a functional role for AgRP neurons in modulating dopamine signaling to drive food intake.

10:15 **Metabolic Signals Shape Learning And Decision-Making (New Investigator Travel Awardee)**

Anne Kuehnel[1], Alica L Guzman[2], Sahiti Chebolu[3], Melina Ghralow[2], Kristin Kaduk[2], Peter Dayan[3,6], Birgit Derntl[2,4], Nils B Kroemer[1,2,4,5]

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To support long-term homeostasis, reward-related behavior is tuned according to the metabolic state of the body. Thus, altered metabolic signaling has emerged as a potential contributor to mental and metabolic disorders. However, despite evidence in animals, the influence of metabolic state over reward-related learning in humans is unproven. Moreover, the effect of differences in metabolic traits (e.g., insulin sensitivity) that may alter this relationship is not yet clear, although it may offer mechanistic insight into disorders. To close this gap, we collected observational and interventional data concerning metabolic scaling of reinforcement learning in a sample of 84 individuals with a wide range of BMI (18 – 36 kg/m^2). First, participants completed up to 60 runs of our App, *Influenca,* assessing learning and value-based decision-making over 4 weeks. At the same time, we performed ecological momentary assessment of metabolic state and continuous monitoring of glucose levels (every 5 min) to differentiate 'objective' and self-reported metabolic state. Using Bayesian mixed-models, we find that average wins depended on the change in glucose levels over the previous 20 min (wins: 95%CI= [-0.69,-0.06]). Second, in an experimental session we manipulated metabolic state via a caloric load (milkshake) vs. water. This increased response times ($p<.001$) and affected learning depending on trait metabolic markers ($p=0.019$). We show that caloric intake can affect how we learn and decide. Crucially, metabolism plays an essential role in scaling reward-related signals according to energy intake. Ultimately, inter-individual difference in the integration of metabolic state related to differences in body composition and metabolic traits will provide insights into adaptive and maladaptive behavioral changes.

10:30 **A Subset Of Pedunculopontine Nucleus Neurons Promote Food Reward**

Nicholas K. Smith, James Bianchi, Ruoxi Wu, Albert, T Yeung, Michelle Awh, Sukya Williams, J. Nicholas Betley
Department of Biology, University of Pennsylvania, Philadelphia, PA, United States

The modern food environment is brimming with advertisements, packaging, and contexts that powerfully drive consumption. As we learn to associate these cues with the palatable and rewarding foods that they predict, the cues themselves gain motivating power over our eating decisions. However, the neural circuits that shape food cue learning are incompletely understood. We hypothesize that an excitatory input to the ventral tegmental area (VTA) mediates the communication of food reward information to dopamine neurons, enabling the associative learning that ascribes appetitive drive to food cues. In mice, we found that the pedunculopontine nucleus (PPN) has a strong connection to the VTA. These PPN neurons that project to the VTA exhibit a robust response to food. Via circuit specific inhibition, we find that this PPN projection is essential for the dopamine response to food reward. Endoscopic imaging identified a specific population of neurons that respond preferentially to food stimuli over other salient stimuli, suggesting the potential for a separable pathway for food reward through the PPN. Using a spatial transcriptomic analysis, we have begun to parse apart genetically and anatomically defined cell types within the PPN. These findings identify the PPN as a critical pathway for food reward to the dopamine system, allowing animals to link environmental stimuli with associated cues. Targeting this pathway could change the motivational impact of eating, limiting the impact of the cues that can lead to tempt unhealthy eating.

10:45 **Amylin Receptor Signaling In The Laterodorsal Tegmental Nucleus (Ldtg) Controls Food Intake Through A Neurotensin Projection To The Ventral Tegmental Area (Vta)**

Marcos J. Sanchez-Navarro, Carlie Zhang, Samantha Fortin, Halcyon Hu, Matthew R. Hayes
University of Pennsylvania, Philadelphia, PA, United States

Research on the role of amylin signaling in the control of energy balance has focused on brainstem and hypothalamic nuclei, leaving other calcitonin receptor (CTR) expressing nuclei such as the mesopontine laterodorsal tegmental nucleus (LDTg) largely understudied. Our lab has shown that LDTg amylin signaling reduces feeding and body weight, but the downstream targets of $LDTg^{CTR}$ cells mediating these feeding effects remain unknown. Interestingly, the LDTg is known to produce the neuropeptide neurotensin (Nts) and activation of Nts receptors in the ventral tegmental area (VTA) reduces feeding and body weight. However, whether $LDTg^{CTR}$ neuron activation reduces feeding via Nts release into the VTA has not been explored. Here, we use circuit tracing techniques to anatomically characterize $LDTg^{CTR}$ neurons and show that a subpopulation of Nts producing $LDTg^{CTR}$ neurons projects to the VTA. Our results also show that LDTg amylin increases VTA cFos activation, suggesting a potential mechanism via which LDTg amylin signaling influences energy balance. To test the functional role of this circuit, we used a dual AAV approach to induce a unilateral circuit specific (LDTg --> VTA) CTR-KD. Our results show that this manipulation is sufficient to attenuate the anorexigenic effects of peripherally-delivered salmon calcitonin, a CTR agonist. Lastly, we used the *Calcr::cre* mouse line to induce projection specific chemogenetic excitation of this $LDTg^{CTR}$ --> VTA pathway and showed that this manipulation is sufficient to reduce food intake and body weight in male and female mice. Altogether, these findings anatomically and functionally characterize a new amylin signaling pathway, further establishing the LDTg as a potential target for novel amylin-based pharmacotherapies to treat obesity.

P364 **Vagus Nerve-Mediated Gut-Brain Signaling Modulates Memory Via Septal Acetylcholine Release: Implications For Diet-Induced Cognitive Dysfunction.**

Logan Tierno Lauer[1], Lea Decarie-Spain[1], Anna Hayes[1], Andrea Suarez[1], Zander Bashaw[2], Molly Klug[1], Alicia Kao[1],

Jessica Rae[2], Keshav Subramanian[2], Kristen Donohue[1], Kevin Myers[3], Scott Kanoski[1,2]

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Consumption of a Western diet (WD) elicits both reductions in gut-to-brain vagus afferent nerve (VAN) signaling and hippocampal (HPC)-dependent memory impairment. However, it is unclear whether the former phenomenon is causally related to the latter. The medial septum (MS) is an anatomical relay between the brainstem and the dorsal HPC, and MS acetylcholine (ACh) neurons extensively innervate the HPC. Thus, we hypothesized that WD-induced disrupted VAN signaling contributes to HPC dysfunction via changes in MS-HPC ACh release. Consistent with this hypothesis, our results reveal that male Sprague Dawley rats chronically exposed to a WD during development demonstrate insensitivity to the food-intake reducing effects of peripheral cholecystokinin administration relative to controls raised on standard laboratory chow. Analyses of eating patterns using BioDAQ automated food intake monitoring further reveals that early life WD-exposed rats also consume larger meals than controls when tested in adulthood. Using *in vivo* fiber photometry and fluorescent ACh sensors (iAChSnFR), we next demonstrate that HPC ACh binding is elevated immediately after consumption of a meal in control rats, but not in rats receiving subdiaphragmatic vagotomy (SDV), ablation of MS ACh neurons (via 1921gG saporin immunotoxin), or in rats exposed chronically to a WD during adolescence. Finally, all three treatments (SDV, MS ACh neuron ablation, and early life WD) lead to analogous impairments in hippocampal-dependent spatial working memory for meal location relative to respective 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.

11:15 **Divergent Patterns Of Dopamine Signaling Responses Between The Hippocampus And The Nucleus Accumbens In Response To Meal Consumption**

Alexander G Bashaw[1,2], Lea Decarie-Spain[1], Logan Tierno-Lauer[1], Alicia Kao[1], Cindy Gu[1], Scott E Kanoski[1,2]

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Dopamine (DA) is a neurotransmitter critically involved in food-related reinforcement learning. While DA signaling in reward-related brain regions such as the nucleus accumbens (ACB) has been widely investigated, far less is known about DA function in the hippocampus (HPC), a brain region known for its role in episodic memory and food intake control. Human PET scans have shown elevated DA binding in the HPC after meal consumption, yet HPC DA binding dynamics over the course of a meal remain unknown. Here, we compared dorsal HPC and ACB (shell) DA binding during meal consumption using in vivo fiber photometry recordings with DA receptor-based fluorescent sensors in adult male Sprague Dawley rats. Photometry recordings revealed differential activity between the HPC and ACB DA binding at meal onset, where DA signal either dynamically decreased (HPC) or increased (ACB) at the first bite of food. Additionally, HPC but not ACB DA binding gradually increased throughout the meal and was significantly elevated in the post-meal relative to the pre-meal state. To directly investigate the role of HPC DA signaling in meal-related episodic memory, another group of rats were implanted with a canula targeting the dorsal HPC. HPC infusion of a DA receptor type 2 (D2R) antagonist immediately following meal consumption impaired meal location memory and reduced latency to consume a subsequent meal, suggesting that HPC DA signaling serves to encode meal-related memories. Collective results identify HPC DA-D2R signaling as a candidate neurochemical mechanism through which nutrient consumption promotes meal-related episodic memory.

11:30 - 1:00 PM	On Own
Lunch	

11:30 - 1:00 PM	Boardroom
PHYSIOLOGY & BEHAVIOR EDITORIAL BOARD MEETING (INVITATION ONLY)	

1:00 - 2:00 PM	L1
MARS Lecture 4 - Marion Hetherington, University of Leeds	

Chair(s): Michelle Lee

1:00 **Playing With Food &Ndash; Cultivating Acceptance For Vegetables In Children Using Learning Theory.**
Marion Hetherington
University of Leeds, LEEDS, United Kingdom

Dietary intakes in children are often low in fruits and vegetables. In the UK fewer than 18% of schoolchildren eat the recommended five-a-day portions of fruits and vegetables. Intake of vegetables is especially low, yet vegetable intake confers long term health benefits beyond those of fruit. To encourage vegetable intake in infants and young children, we have conducted a series of experiments to test the efficacy of repeated exposure on weighed intake of vegetables in young children (during complementary feeding; at snack time in pre-schoolers). Whilst familiarisation is effective in increasing acceptance of vegetables, especially in infancy, we have also tested the impact of experiential learning, including sensory play and exploration, on intake and willingness to try vegetables. In a recent, cluster-randomized controlled trial with two arms (control vs intervention) we tested the effect of sensory food education on willingness to try vegetables in school age children. The intervention did not have the expected effect, instead, contextual facilitation increased willingness to try new foods across both arms. A consistent finding across these studies is the importance of individual differences, the naturalness of the eating environment and the social context of food exposure on outcomes. Promoting intake of vegetables can be achieved in several ways, taking account of the characteristics of the child (including age), type of eating episode (meal vs snack) and social context.

2:00 - 2:50 PM	L1
Business Meeting	

All are welcome and encouraged to attend.

Chair(s): Mitchell Roitman

2:00 **President**
Mitch Roitman

2:07 **Secretary/Membership**
Kevin Myers

2:14 **Treasurer**
Will de Lartigue

2:21 **Long Range Planning**
Jessica Santollo

2:28 **Program Committee**
Carrie Ferrario

2:35 **New Investigator Advisory Committee**
Magen Lord

2:42 **New Business**

3:00 - 4:30 PM	L1
Awards Session	

P2 3:00 **Kevin Myers - Hoebel Prize For Creativity, Introduction By Ann-Marie Torregrossa**
Kevin Myers

P3 3:30 **Lindsey Schier - Alan N. Epstein Research Award, Introduction By Alan Spector**
Lindsey Schier

P4 4:00 **Margaret Morris - Distinguished Career Award, Introducton By Thomas Lutz**
Margaret Morris

7:00 - 11:00 PM	Offsite - Museum of Natural History
AWARDS CEREMONY & CLOSING BANQUET (FULL REGISTRATION REQUIRED)	

The 2025 Awards Ceremony & Closing Banquet will take place at The Oxford University Museum of Natural History. Tickets are required and will be noted on your name badge with a wine sticker. Please bring your name badge/ticket to the event.