



33rd Annual Meeting of the Society for the Study of Ingestive Behavior

Printable Program and Abstracts

August 5 - 9, 2026
Philadelphia, PA

Wednesday, August 5, 2026

1:00 - 3:00 PM	Lescaze
SSIB Board Meeting (Invitation Only)	

1:00 - 5:30 PM	Regency Foyer
Registration	

3:45 - 5:00 PM	Millennium Hall
MARS Lecture 1: Camilla Nord	

Chair(s): Grace Shearrer

3:45

Opening Greetings

Kathleen Keller

4:00

Energy Allostasis: Uncovering The Hidden Link Between Metabolic And Mental Health

Camilla L. Nord

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To survive, our brain must accurately predict internal states, enabling flexible, prospective regulation of the body's physiology, or 'allostasis': eating before starvation, drinking before dehydration. Wide-ranging studies report a disruption in allostatic mechanisms in mental health disorders, potentially driving clinical features such as appetite dysregulation in major depression as well as known epidemiological comorbidity between depression and poor metabolic health. I will discuss a series of cognitive-computational neuroscience experiments investigating the overlap between mental and metabolic health, including finding that depression and diabetes are both associated with disruptions in effort-based decision-making, and that mental and metabolic health is associated with changes in reinforcement learning. I will situate these cognitive mechanisms in a broader model of energy allostasis as a link between disruptions to metabolism and mental health.

5:00 - 6:30 PM	Regency Foyer
Opening Reception & Exhibits	

Thursday, August 6, 2026

8:00 - 5:30 PM	Regency Foyer
Registration	
9:00 - 10:00 AM	Regency C & Foyer
Poster Session 1, Exhibits & Coffee Break	

International Foundational Honorees

Harry Kissileff, Suzanne Higgs, France Bellisle, Anton Scheurink, Kent Berridge

SSIB has agreed to preserve the memory of scientists from four countries outside the United States whose early scientific contributions enabled the society to achieve international status. Their foundational research encouraged investigation of ingestive behavior as a distinctive scientific discipline with international collaborations. The scientists and their contributions are listed below in alphabetical order by last name, and will appear on a poster at the 2026 meeting in Philadelphia. **From UK** **Steve Cooper's** methodical approach to the study of ingestive behaviour combined a thorough knowledge of pharmacology with detailed study of behaviour and ethology. His systematic studies of benzodiazepine and opioid effects on eating defined the neurochemical basis of palatability. Other important contributions include the characterisation of the mechanisms underlying the effects of dopamine agonists and antagonists on feeding and functional interactions between cholecystokinin and serotonin in the control of satiety. **From France** After contributing to major developments in sensory physiology (particularly in olfaction and taste), **Jacques Le Magnen** investigated the regulation of energy and hydromineral balances. His studies of food/fluid intake in laboratory rodents established the existence of biological cycles (day/night; meal-to-meal) that affect both ingestive behaviors and the energy status of the body. The "edogram" (an objective recording of ingestive patterns at mealtime in humans) is one of his many contributions to the study of human behavior. **From the Netherlands** (pending) **From Israel**, **Jacob Steiner's** ground-breaking studies of taste-elicited facial expressions in human newborns, showed that expressions to sweet, bitter, and other tastes resolved into hedonic categories of positive 'liking' vs negative 'disgust', and demonstrated the same expressions occurred in anencephalic infants. Steiner's work revealed a brainstem competence for taste sensory identification and basic affective reactions and led to subsequent analyses of taste-reactivity neural mechanisms by Grill, Norgren, and others.

P101

Texture-Dependent Variation In Inter-Bite Pauses And Their Relation To Eating Rate And Food Intake

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Inter-bite pauses differ across food textures, but their relevance to total food intake is uncertain. This study tested whether mean inter-bite pause duration (IBPD) predicted total food intake during a four-course meal and whether effects differed for hard (HF) versus soft foods (SF) or if they varied by chewing, sex, or BMI. Thirty adults (age=27.1±7.8y; BMI 18.3–38.9 kg/m²; 63.3% female) individually consumed a standardized laboratory lunch that was video-recorded for detailed analysis of oral-processing behaviors. Frame-by-frame coding captured bites, chews, chews-per-bite, IBPD (seconds, s), eating rate (g/min), and total meal duration (TMD, min). Foods were weighed before and after consumption to determine total food intake. IBPD was computed at the individual level for the full meal and separately for HF and SF. Hierarchical regressions, with covariates entered in a priori blocks (chews-per-bite, eating rate, TMD, sex, BMI), tested whether IBPD predicted TFI. Additional models examined texture-specific inter-bite pause effects and pause×BMI interactions. IBPD was significantly longer for SF than HF (SF=18.8s, HF=13.4s), $t(29) = -5.35$, $p < .001$. Across all models, eating rate ($B \approx +11-12$, $ps < .001$) and TMD ($B \approx +11$, $ps < .001$) were strong positive predictors of total food intake, explaining over 90% of variance ($R^2 \approx .91$). IBPD, chews-per-bite, and sex did not significantly predict total food intake in any of these models, nor did pause×BMI interactions. In summary, SF produced longer IBPD than HF, but IBPD did not independently predict food intake once eating rate and TMD were controlled. Total food intake was driven by how fast and how long participants ate, not by how long they paused. IBPD is texture-sensitive, but it was not related to food intake in this context.

P103

Dining Out In Nyc: Investigating The Influence Of Multisensory Urban Design Factors On Eating Behavior With Vr

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Premise WHO's "Healthy Cities" initiative emphasizes the need to consider health impact when planning urban infrastructure, including restaurant design. Sensorial factors such as taste or visual aesthetics in a restaurant can influence eating behavior. Less researched, olfactory cues may also directly or indirectly alter eating behavior. Understanding the impact of smells on eating behavior could inform city regulations to support healthy habits within restaurants. *Hypothesis* Eating in the presence of an unpleasant smell will increase negative emotions, resulting in increased food intake and reduced mealtime when compared to a pleasant smell. *Procedures* 25 participants in a pilot randomized crossover trial attended two lab visits in counterbalanced order to receive the pleasant or unpleasant smell. Participants reported their mood and perception of the smell multiple times during each visit and consumed a standardized lab meal. Mean differences in mood, total food consumed, and length of meal were compared between scent conditions using paired t-tests. Linear mixed models were used to control for interacting factors. All statistics were run with SPSS. *Results* Although the smell conditions differed in perceived pleasantness ($t=6.451$, $p<0.001$), we did not observe a statistically significant difference in total energy of food consumed ($t=-0.993$, $p=0.331$) or length of meal ($t=0.867$, $p=0.395$) between conditions. Changes in smells also did not cause a significant change in mood (all p -values >0.05). *Conclusion* Current findings indicate that environmental smell alone may not be sufficient to manipulate eating behavior, but larger studies with more power to detect differences may better identify how various smell types and strengths might influence eating behavior and health.

P105 **Exendin-4-Phe1 Reduces Opioid-Mediated Behaviors And Opioid-Evoked Dopamine Levels In The Nucleus Accumbens Of Rats.**

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Given the continued prevalence of fatal overdoses associated with opioid misuse in the United States and the limitations of current FDA-approved treatments, there is an urgent need for novel pharmacotherapies to treat opioid use disorders (OUDs). Emerging studies show that glucagon-like peptide-1 receptor (GLP-1R) agonists attenuate the rewarding and reinforcing effects of addictive drugs, including opioids, in rodents and humans. Our preliminary studies indicate that Exendin-4-Phe1 (Ex-Phe1), a biased GLP-1R agonist, attenuates opioid-taking and -seeking behaviors at doses that do not produce malaise-like effects in rats. This study aims to elucidate the neurobiological mechanisms underlying the efficacy of Ex-Phe1 on opioid-mediated behaviors. We hypothesize that Ex-Phe1 will reduce opioid-evoked dopamine levels in the nucleus accumbens (NAc) of rats. Male ($n=4$) and female ($n=1$) Sprague-Dawley rats were surgically implanted with indwelling jugular catheters and injected with an adeno-associated virus expressing GRAB_DA1h, a dopamine sensor, into the NAc shell. Following a recovery period, rats were pretreated with vehicle or Ex-Phe1 (3 or 10 $\mu\text{g/kg}$, i.p.) before an acute priming injection of fentanyl (2.5 $\mu\text{g/kg}$, i.v.). GRAB_DA1h fluorescence was measured in the NAc using *in vivo* fiber photometry. Area under the curves (AUCs) and maximum z-scores were analyzed using one-way ANOVAs. Our pilot studies suggest that Ex-Phe1 may attenuate opioid taking, in part, by dose-dependently decreasing fentanyl-evoked dopamine levels in the ventral striatum. Future studies will optimize dosing regimens of Ex-Phe1 and assess the efficacy of GLP-1R biased agonists on drug-seeking behaviors during abstinence in opioid-experienced rats.

P107 **Gradual Sugar Reduction Decreases Sugar Intake Without Changing Product Liking Or Amount Eaten**

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Overconsumption of sugar, especially in sugar-sweetened beverages, is associated with health risks like obesity, diabetes, and cardiovascular disease. Our objectives were 1) determine how sugar-sweetened iced tea liking would change over time for people in a gradual reduction of sugar group compared to those in a control group, 2) determine if changes in liking ratings from the initial to the final taste test differed between the two groups, 3) determine if participants in the gradual reduction group increased their liking of lower sugar concentrations. Participants that consumed sweetened tea at least three times per week enrolled in this three-phase study: an initial taste test, a 12-week repeated consumption phase, and a final taste test. At the initial and final taste tests participants were served teas differing in sugar content. We divided participants into a control or a gradual reduction group for the 12-week repeated consumption phase by balancing the groups for their initial hedonic sensitivity to sweetness and their motivation to decrease their dietary sugar intake. The control group received a 7.7% sugar-sweetened tea for the duration of the 12 weeks. The gradual reduction group received a tea that was reduced weekly in increments of 10% of the previous week's sucrose concentration. Over the consumption phase, liking decreased gradually and equally for the control and gradual reduction groups. From the initial taste test to the final taste test the lowest acceptable, ideal level, and the highest acceptable level of sweetness did not differ between the control and gradual reduction group.

P109 **Food Availability Elevates Cortisol Stress-Reactivity In Women With High Dietary Restraint**

Naomi J McKay¹, Taha H Ghadeer¹, Cecelia A Redding¹, Brittany L Campanella¹, Brent P Howes¹, Lillyan P Kingsbury¹, Tamari-Rose Love¹, Kavorn F McKoy¹, A. Janet Tomiyama²

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Eating during a laboratory stressor has not been found to reduce stress reactivity. It is possible that any anxiolytic properties of food may be specific to a subpopulation. Those high in cognitive dietary restraint are more likely to elevate energy intake in response to stress and, therefore, may be more impacted by any eating-associate anxiolytic effects. To test this, it was hypothesized that 1) food provided during anticipation of a stressor will blunt stress reactivity in women with high restraint and 2) those with high restraint will have higher energy intake in response to stress. Participants (n=87; women ages 18-30), provided baseline measures of stress (self-rated anxiety and salivary cortisol), and engaged in either the Trier Social Stress Test or a No Stress condition. Participants also were randomly assigned to have a basket of “complimentary snacks” available for 10 minutes either during stress anticipation or after the stressor. Stress measures were taken throughout, and energy intake was recorded. When anxiety was examined, there was no interaction between Stress, Restraint, and Food Timing and no main effect of Restraint. There was, however, an interaction between Stress, Restraint, and Food Timing on cortisol ($F(1.76, 118.1) = 3.83, p = .03$). In high restraint, access to food during stress anticipation caused an elevation in cortisol post-stress, but there was no elevation when food was only available after the stressor. Those with low restraint exhibited an opposite pattern. There was no effect of restraint on energy intake. These results suggest that access to food influences physiological stress reactivity while not impacting the emotional reaction to stress and that there are differential effects in those with low or high restraint.

P111 Cisplatin Induces A Conditioned Taste Aversion In Mice That Is Not Mitigated By Ondansetron, Elaborating On A Behavioral Model To Study Causes And Treatments Of Nausea

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Nausea is a common symptom, yet understanding of its pathogenesis and optimal treatments remains elusive, due partly to limitations in the animal models of nausea. Conditioned taste aversion (CTA) has been used in rats to demonstrate the effectiveness of nausea treatments, but few CTA studies have been conducted in mice, and none of them have assessed nausea treatments. We hypothesized that clinical nausea is closely modeled by CTA in mice, as it is in rats. Into 8-12 month old C57B6 mice (n = 83), we implanted intraoral (IO) cannulas; on subsequent consecutive days, they underwent 5 conditioning sessions, habituation, and then testing. During conditioning, 0.1% saccharin was infused IO, followed by IP administration of saline, cisplatin (0.5 or 2.5 mg/kg body weight), or lithium chloride. In each exposure group, half the mice were pre-treated with ondansetron 0.2 mg/kg IP 30 minutes before conditioning. In the testing session, behaviors during saccharin exposure were video recorded and manually scored. Compared to saline control, cisplatin conditioning at either dose decreased the proportion of taste reactivity behaviors that represented appetitive responses ($P = 0.0028$, U test). However, pre-treatment with ondansetron did not significantly alter this measure in any of the nausea exposure conditions. This study demonstrates, for the first time, that cisplatin elicits nausea-like behavior in mice, but pre-treatment with ondansetron does not mitigate this effect. Our findings establish the value of the CTA paradigm in the broader exploration of nausea and conditioned aversion in mice, especially in the context of transgenic approaches to elucidate relevant neural pathways; they also highlight CTA's limitations when evaluating new and established therapies for nausea.

P113 Restrictive Food Parenting Practices Predict Loss-Of-Control Eating In Children With Healthy Weight, But Not In Those With Overweight/Obesity, During A Buffet-Style Test Meal

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Loss of control (LOC) over eating is defined as the subjective feeling of a lack of control over eating. While restrictive food parenting practices are associated with child overeating and eating in the absence of hunger, less is known about the relationship with child-reported LOC. This study aims to examine the relationship between restrictive food parenting practices and child-reported LOC eating in a buffet-style test meal. Participants include 106 children ages 8 – 11 (51% girls) and a parent. Food parenting was assessed using parent reports on the Structure and Control in Parent Feeding Questionnaire. Children completed a buffet-style test meal and reported on their LOC eating during the test meal. Child height and weight were measured and used to categorize participants as having healthy weight (HW) or overweight or obesity (OW/OB). Logistic regression models were used to examine how restriction predicted LOC after the test meal in those with 1) HW, and 2) OW/OB. Restriction positively predicted reported LOC eating during the test meal in children with HW ($p = .041$), but not in children with OW/OB ($p = .649$). There is a well-established link between parental restriction and disordered eating behaviors, so the results in children with HW are unsurprising. However, the results in children with OW/OB indicate that parental restriction has no impact on reported LOC eating at the test meal. These data suggest that children with OW/OB may be less sensitive to parental restriction or that LOC eating is related to other unstudied factors. Future research should assess other potential triggers of LOC eating in children with OW/OB.

P115 Not All Food Is The Same: Glucagon-Like Peptide-1 Receptor Agonists Associated With Selective Reduction Of Ultraprocessed Food Reward

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Glucagon-like peptide-1 receptor agonist (GLP-1RA)-based therapies have reshaped obesity and type 2 diabetes treatment. Yet research investigating their impact on food reward has largely ignored meaningful differences between ultraprocessed foods (UPFs), engineered to heighten reward salience, and minimally processed foods (MPFs). In an exploratory study, 328 human adults using semaglutide or tirzepatide for ≥ 3 months (74.4% women; 22-76 years) retrospectively reported pre-treatment and current food addiction (FA) symptoms (modified Yale Food Addiction Scale 2.0; 0-11), food noise (Food Noise Questionnaire; 0-20), and cravings for and enjoyment of UPFs and MPFs (0-100 visual analog scales). Data were analyzed using paired t-tests, MANOVA, and regressions with pre-post change scores. Reports of FA symptoms decreased from pre-treatment ($M=4.5$) to current ($M=1.1$), $p<.001$, 95%CI [3.1, 3.8]. Reductions in food noise were greater for UPFs ($\Delta M=7.8$, baseline $M=11.0$) than MPFs ($\Delta M=0.9$, baseline $M=3.3$), $p<.001$, 95%CI [6.1, 7.6] following treatment. A within-subjects 2x2 MANOVA revealed a large main effect of food type: UPF craving and enjoyment ratings decreased ($\Delta M=42.1$ and 38.0), whereas MPF craving and enjoyment ratings increased ($\Delta M=-14.3$ and -15.6) following GLP-1RA initiation ($p<.001$, $\eta^2=0.60$). Change was greater for cravings than enjoyment ($p=.019$, $\eta^2=0.02$). In separate regressions, UPF-specific change variables (food noise, cravings, enjoyment) each significantly predicted current FA symptoms above baseline, while MPF variables did not. Findings suggest GLP-1RAs may selectively reduce UPF-related reward salience, informing how these medications reshape food reinforcement and highlighting the need for food-specific frameworks in GLP-1RA research.

P117 **Cognitive Restraint Is Associated With Reduced Energy Intake From Ultra-Processed Foods In An Inpatient Controlled Feeding Study**

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Ultra-processed foods (UPFs) promote excess energy intake (EI), weight gain, and dominate the current food environment. Eating behaviors are shaped by many factors, but susceptibility to overeating varies across individuals. We explored whether personality and eating traits explain differences in excess EI from a diet high in UPFs, energy density (ED), and hyper-palatability (HP). We hypothesized that higher cognitive restraint (CR) and conscientiousness and lower reward-based eating, disinhibition, and neuroticism would be associated with lower *ad libitum* EI on a UPF diet. In a randomized crossover inpatient feeding trial, healthy weight-stable adults ($n = 36$; age 36.3 ± 11.3 years; BMI 29.5 ± 7.0 kg/m²) consumed 7-day *ad libitum* diets matched for provided energy, macro/micronutrients but varying in ED, HP, and proportion of UPF. Here we report on: (1) high ED/HP with 80% kcal from UPFs, and (2) low ED/HP with no UPFs (minimally processed diet, MPF). Excess EI was defined as the difference in intake between the diets, adjusted for resting energy expenditure via indirect calorimetry. Personality and eating traits were assessed via validated questionnaires at standardized times. Significant associations met Spearman rank alpha of 0.05. Participants consumed 948 ± 419 kcal/day more on the UPF diet compared to MPF (95% CI 807–1090 kcal). Despite extant evidence suggesting links between conscientiousness, reward-based and disinhibited eating with weight status and EI, our exploratory results highlight a link between greater CR on the Three Factor Eating Questionnaire and lower excess EI on the UPF diet ($q = -0.34$, $p = 0.04$). Interventions to strengthen CR may be useful tools to optimize weight management in UPF-rich environments.

P119 **U-Shaped Relationship Between Exploration-Exploitation Tendencies And Consumption Of Sugar-Sweetened Beverages In Adolescent Girls**

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How individuals learn about rewarding foods is hypothesized to underlie excess caloric consumption. We tested if differences in reward learning cognitive processes, learning from positive or negative feedback (α_{gain} and α_{loss}) and tendency to explore or exploit reward options (β), were associated with intake of sugar sweetened beverages (SSB). We expected that high exploration (low β) would be positively related to SSB intake. 36 healthy girls (age=12.5y $\pm$ 2.8y, body mass index percentile =58.3 $\pm$ 33.1, SSB=105.8 $\pm$ 121.6 gr/day) completed 12 24-hour dietary recalls over 6-months to assess SSB intake. Participants completed a novel candy reward probabilistic selection task (PST) to assess reward learning cognitive processes. Participants were presented 3 pairs of symbols with varying probabilities of an M&M or Skittle reward (AB pair: 80%, 20%; CD pair: 70%, 30%; EF pair: 60%, 40%). We fit a hierarchical Bayesian Q-learning model to PST choice data to derive learning parameters (α_{gain} , α_{loss} , β). We used Bayesian model averaging to test the association between SSB intake and α_{gain} , α_{loss} , and β , controlling for demographic covariates. We found a quadratic relationship between β and SSB intake (posterior inclusion probability =96.86, Bayes Factor (BF) =15.65). A BF between 10-30 is considered strong evidence of a relationship. The presence of an “U-shaped” quadratic relationship between SSB intake and β , the explore-exploit parameter is in line with previous work showing that an optimal cognitive function is between a low and high dopamine (DA) states. Since DA underlies explore-exploit decision making, we may be capturing a behavioral correlate of DA associated with excess caloric intake.

P121 **Circadian Analysis Of Food Intake In *Rgs7Bp* Knockout Mice Prone To Increased Adiposity**

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Obesity affects ~108 million American adults; current medications require ongoing use with substantial side effects. In rodent models, we identified *Rgs7bp*, encoding the regulator of G protein signaling 7 binding protein, as a novel target for diet-induced obesity. RGS7BP variants associate with BMI, body weight, chronotype, and insomnia in human GWAS. Here, accordingly, we study circadian feeding in male and female *Rgs7bp* wildtype (WT) ($n=31$) and knockout (KO) ($n=29$) mice, which are prone to increased adiposity (by 8 weeks old, $b=3.08\%$ body fat, $p<.0001$). For Training Phase (15 days), adult single-housed mice free-fed on 5TUM (3.30 kcal/g; 10.4% fat; 10% fructose) via FED3 devices. For Diet Phase (8 weeks), mice then received *ad lib* access to: 1) 5TUM, 2) sweet-fat

(SF; 4.18 kcal/g; 35% fat; 31% sucrose), or 3) intermittent SF access (24 hr, 3 d/week) with less preferred 5TUM on non-access days. Intake (1-hr bins) was individually fit to a 2-harmonic cosinor regression (R). In Training Phase, KO mice had an earlier 2nd-harmonic acrophase ($p<.05$) and reduced peak ($p<.05$). Female, but not male, KO ($p=.0001$) had earlier nadir times (Sex X Genotype, $p<.05$). In Diet Phase, KO mice had smaller 2nd-harmonic amplitudes ($p<.05$), greater nadirs ($p<.05$), and an earlier time at nadir ($p<.01$) on access days. On non-access days, KO mice had smaller 2nd-harmonic amplitudes ($p<.05$), smaller peaks ($p<.05$), and an earlier time at nadir ($p<.001$). Pre-existing genotype differences in body fat (%) persisted at week 8 ($p<.001$) and KO mice gained more body weight than WT over the study period ($p<.05$). Overall, KO mice show a blunted circadian rhythm of feeding with smaller amplitude caused by lower peaks and higher nadirs, which may contribute to their increased body weight and adiposity.

P123

The Role Of Calcineurin In Increasing Calcium-Permeable Ampa Receptor Recruitment In The Nucleus Accumbens.

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External cues associated with fatty and sugary foods trigger food craving and can promote overeating that contributes to weight gain and rising obesity rates. Activity of neurons in the nucleus accumbens (NAc) play a critical role in mediating these cue-induced urges to eat. For example, activity of excitatory calcium-permeable AMPA receptors (CP-AMPA) in the NAc is required for cue-triggered food-seeking. Consumption of a sugary, fatty junk food (JF) diet is sufficient to increase NAc CP-AMPA and cue-triggered food seeking (unpublished observation). However, how NAc CP-AMPA increases occur is poorly understood. Here we determined whether inhibiting the calcium-dependent protein phosphatase calcineurin (CaN), which prevents CP-AMPA synaptic incorporation in other brain regions, is sufficient to enhance NAc CP-AMPA transmission. We used patch-clamp electrophysiology to assess whether pretreatment with the CaN antagonist FK506 (5 μ M) increases NAc core CP-AMPA transmission in obesity-prone male rats. Initial results suggest that FK506 tends to increase CP-AMPA as indicated by a greater ability of the CP-AMPA antagonist Nasp (200 μ M) to reduce evoked EPSC amplitude. In addition, a larger proportion of neurons in the FK506 group showed a strong Nasp sensitivity (>20% reduction) compared to controls ($n = 9/18$ FK506, 4/18 control cells). Ongoing studies will determine whether FK506-responsive cells are specific to D1-type or D2-type medium spiny neurons. We will also use western blotting to determine whether FK506 increases NAc CP-AMPA phosphorylation, which mediates CP-AMPA surface expression. These studies provide foundational information about the mechanisms that regulate NAc CP-AMPA and will provide insights into CP-AMPA recruitment following JF diet.

P125

The Effects Of Amylin On The Antimicrobial Activity Of Amyloid Beta And Its Implications In Ingestive Behaviors And Alzheimer'S Disease

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Rationale/Premise: Amylin is a satiety protein that is secreted from pancreatic beta cells. In addition to its normal function in satiety, dysfunctional amylin is known to contribute to the development of Type II diabetes through the formation of protein aggregates that disrupt the cell membrane and result in pancreatic beta cell dysfunction. The protein aggregates formed by amylin in pancreatic beta cells have similarities to the aggregates formed by amyloid beta in neuronal cells. Amylin and amyloid beta have both been identified as being involved in Alzheimer's disease and having antimicrobial protein (AMP), which is significant because AMP activity may be linked to Alzheimer's disease. **Hypothesis and Species:** This study hypothesized that amylin acts as a regulator of Ab AMP activity in the presence of gram-positive bacteria *S. epi*. **Procedures:** *S. epi* was diluted to a concentration of 0.063 (McFarland standard). *S. epi* was mixed with amylin, Ab, or amylin + Ab. Serial dilutions were conducted. The various dilutions were streaked on an agar plate and incubated overnight. Each protein combination was tested for growth. Bacterial cells were counted on each plate and Graph Pad Prism was used for analysis. **Results:** The plates with *S. epi* + Ab demonstrated less growth than the control of *S. epi*. The plates with Ab and amylin together showed less growth than the control as well, corroborating with other studies showing amylin as an antimicrobial protein as well, as well as showing amylin as having an effect on Ab amp activity. **Conclusion:** Amylin is shown to stop the growth of gram-positive bacteria. This study suggests that amylin can increase the ability of Ab's function, which may influence the involvement of both proteins in Alzheimer's disease.

P127

Effects Of A Long Lasting Gipr Agonist In Models Of Ingestive Behavior And Psychostimulant Reward

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Food and psychostimulant drugs of abuse engage overlapping neural circuits, yet their functional integration remains poorly understood. Cocaine-driven adaptations in dopamine (DA) pathways dysregulate behavior, but emerging evidence suggests that incretin-based therapeutics can modulate these same reward circuits. As a dual GLP-1R/GIPR agonist, tirzepatide highlights the potential of combined incretin signaling to influence reward-related processes. Whether GIPR agonism alone influences cocaine-associated behaviors; however, remains unknown. We hypothesized that GIPR activation using the long-acting GIPR agonist, [d-Ala²] GIP₁₋₄₂, modulates cocaine-induced reward, locomotor sensitization, and feeding. Adult male and female wildtype C57BL/6J mice underwent a conditioned place preference (CPP) protocol with either saline and cocaine (20 mg/kg) on alternating days. On the test day, mice were randomized and injected

with saline or 50 µg/kg [d-Ala²] GIP₁₋₄₂ prior to chamber exploration. While both groups showed a significant preference for the cocaine-paired chamber, [d-Ala²] GIP₁₋₄₂ produced a significant decrease in the time spent in the drug-paired context. We then assessed cocaine-induced locomotor sensitization across repeated cocaine exposures and feeding using a fast-refeed paradigm. GIPR monoagonism attenuated cocaine-induced locomotor sensitization and feeding after a 24-hour fast. These findings suggest that GIPR signaling regulates psychostimulant and ingestive behaviors, potentially via modulation of DA circuits. In future studies, we will examine the impact of GIPR agonism on voluntary cocaine self-administration. Targeting GIPR may represent a novel strategy to address cocaine use disorder while simultaneously impacting energy balance and feeding dynamics.

P129

Effects Of Calories, Sweetness And Caffeine On Metabolic Responses And Flavour Nutrient Conditioning In Humans

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Sugar-sweetened beverages often contain caffeine, a stimulant that promotes dependence and increased intake. Despite frequent co-consumption, how sugar and caffeine jointly strengthen learned flavour preferences is unclear. This pilot study investigates how sugar and caffeine, alone and in combination, shape flavour preferences through perceptual, metabolic measures and fMRI. 10 participants underwent a flavour–nutrient conditioning protocol using four beverage conditions: 1) sweet/no calories (sucralose), 2) sweet/calories (sucralose+maltodextrin), 3) sweet/no calories/caffeine (sucralose+ caffeine) 4) sweet/calories/caffeine (sucralose+maltodextrin+caffeine). Each beverage was made with a distinct novel flavour and colour. At baseline, liking ratings, indirect calorimetry and blood were collected pre/post-consumption to quantify liking, energy expenditure (REE), substrate oxidation (RQ), and circulating glucose. fMRI and liking were assessed after participants consumed each beverage 5 times (over 20 days). At baseline linear mixed models revealed a shift toward carbohydrate oxidation ($p = 0.0007$) and increased blood glucose ($p = 0.0006$) after consumption of drinks containing maltodextrin. Caffeine had no influence on this effect. We also identified a main effect of time for all drinks ($p = 0.0005$), such that REE increased following consumption regardless of drink ingredients. Accordingly, the time * interaction comparison was not significant ($p = 0.4$). Conditioning had no effect on liking and neuroimaging analyses are ongoing. These results support the feasibility of our design for a larger study and suggest that 1) caffeine does not influence metabolic response to calorie ingestion and 2) sweet taste alone is sufficient to induce an increase in energy expenditure.

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Tirzepatide Dampens Motivation For Palatable Food With Minimal Effects On Hedonic Processing

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The GLP-1/GIP dual analog tirzepatide is the most effective FDA-approved weight loss pharmacotherapy to date, yet the neurobehavioral mechanisms mediating its effects on food intake remain poorly understood. Here, we examined how tirzepatide influences appetitive and consummatory processes associated with palatable food. In male rats given a two-choice diet, acute systemic tirzepatide selectively reduced caloric intake from a high-fat, high-sugar (HFHS) diet without affecting chow consumption. To determine whether this reflects altered hedonic processing, a taste reactivity test was used. Analysis revealed a modest but significant shift in sucrose-evoked hedonic responses following tirzepatide treatment, characterized by fewer high-intensity tongue protrusions and an increase in lower-intensity hedonic mouth movements, without signs of aversive responses or a reduction in total hedonic responses. We then assessed effort-based motivation using an operant progressive ratio reinforcement task for HFHS pellets. Acute tirzepatide dose-dependently reduced breakpoint and active lever presses, indicating a robust decrease in motivation to work for palatable food. Finally, to assess mesolimbic dopamine dynamics during cue-driven behavior, we expressed a dopamine sensor in the nucleus accumbens medial shell and recorded dopamine binding during a Pavlovian discrimination task (CS+ predicting liquid sucrose; CS– non-reinforced). Our results revealed that tirzepatide attenuated the decline in dopamine following sucrose delivery. Collectively, these findings demonstrate that tirzepatide selectively suppresses palatable food intake primarily through reduced motivation and is associated with altered mesolimbic dopamine signaling during reward consumption.

P133

Single-Nucleus Transcriptional And Chromatin Accessibility Profiling Of Mouse Hypothalamic Leprb Neurons Reveals Cell Type-Specific Cis-Regulatory Elements Linked To Human Obesity

Rationale: Leptin receptor-expressing hypothalamic neurons (LepR^{Hypo}) are key regulators of energy balance, yet a comprehensive, cell type-resolved chromatin accessibility map of these neurons is lacking. Defining the cis-regulatory architecture of LepR^{Hypo} subtypes may reveal pathways governing body weight and candidate regulatory elements relevant to obesity. Hypothesis: Distinct LepR^{Hypo} neuronal subtypes exhibit unique chromatin accessibility landscapes, including conserved cis-regulatory elements linked to human obesity-related traits. Species: Mouse (*Mus musculus*). Number of Subjects: 6 female mice. Procedures:

~20,000 pooled LepR^{Hypo} nuclei were used for single-nucleus multiome (snRNA-seq/snATAC-seq). Integrated analyses identified clusters and cluster-specific open chromatin regions (OCRs). Mouse-to-human orthology mapping with obesity GWAS and eQTL integration identified conserved regulatory elements linked to obesity-related traits. Results: We identified 39 transcriptionally and epigenetically distinct clusters, including AgRP, Pomc, Foxb1, Irx5/3, Nts, PNOC, Kiss1/Pdyn, Ghrh, Tcf7l2, and Sf1/Nr5a1 populations. Three Glp1r-expressing clusters showed the highest Lepr enrichment and distinct molecular signatures.

Cluster-specific OCRs delineated putative cis-regulatory elements unique to LepR^{Hypo} subtypes. Conserved mouse OCRs mapped near genes with high Human Genetic Evidence scores for obesity-related traits and overlapped obesity-associated GWAS loci and/or eQTLs. Conclusions/Relevance: These data provide a cell type-specific cis-regulatory atlas of LepR^{Hypo} neuronal subtypes and highlight conserved regulatory elements, candidate genes, and putative functional variants that may influence energy homeostasis and obesity susceptibility in humans.

P135

Acute Effects Of Glp-1, Amylin Agonists And Their Combination On Phasic Dopamine Signaling

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Dopamine has been hypothesized to promote energy intake by reinforcing eating, amplifying food seeking, and establishing learned associations with palatable food. GLP-1 receptor agonists (GLP1-RAs) administered either peripherally or centrally, attenuate food intake and measures of reinforced eating behaviors. Amylin RAs (AmyRAs) also cause weight loss and decreased motivation for food. Dual agonism results in more effective weight loss. Unknown is whether acute, systemic administration of GLP-1RAs, AmyRAs or combination affect phasic dopamine signaling – an important contributor to food reinforced behaviors. We trained ad libitum-fed rats (n=9) on a Pavlovian paradigm, where each of five different auditory cues predicted a unique frequency of stimulation to the medial forebrain bundle via a chronically implanted electrode. Fluctuations in dopamine release were measured in the nucleus accumbens core using expression of the fluorescent sensor dLight1.3b and fiber photometry. Cue and stimulation responses stabilized over 10 daily sessions. Vehicle was injected before (t-15min) session 11 and agonist (semaglutide, 10nmol/kg; cagrilintide, 10nmol/kg; combo 2nmol of each) before session 12. After 1 week, the next vehicle-agonist sessions were run. All treatments reduced 24hr body weight. Only cagrilintide exhibited modest effects on dopamine signaling – reducing electrically- but not cue-evoked dopamine release. Results are compared to amphetamine and a kappa-opioid receptor agonist – which were effective in modulating dopamine. Taken together, these data indicate that acute, clinically relevant doses of GLP-1RAs and AmyRAs have minimal impact on phasic mesolimbic dopamine signaling, with only modest effects observed for cagrilintide on electrically evoked release.

P137

Changes In Anxiety-To-Eat Distinguish Responders From Non-Responders To Nutritional Rehabilitation

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Individuals with anorexia nervosa (AN) often experience marked anxiety to consume foods high in energy density (HED). We previously showed that this anxiety-to-eat is portion size-dependent and improves with meal-based weight restoration treatment. Whether nutritional rehabilitation shifts this dose-response curve uniformly across patients remains unknown. Here we constructed anxiety-to-eat response curves to images of five portion sizes (0.25, 0.5, 1, 2, and 4) of HED foods collected at hospital admission and prior to discharge in inpatients with AN and atypical AN (N=22). Changes in anxiety-to-eat were analyzed using K-means clustering to identify treatment response subgroups based on patient-level response curves. Two subgroups were identified: a treatment responsive group (“responsive”, n=11; mean reduction in anxiety-to-eat = 13.0 points + 5.1 points) and a “non-responsive” group (n=11; mean reduction in anxiety-to-eat = 0.9 points + 3.2 points). The groups did not differ at baseline in eating, shape, or weight concern or eating restraint as measured by the Eating Disorder Examination Questionnaire. However, the “responsive” group had greater baseline anxiety-to-eat than the “non-responsive” group, with no between-group differences remaining after treatment. No other clinical or diagnostic variables predicted group membership or correlated with changes in anxiety-to-eat. These findings demonstrate differential responses to nutritional rehabilitation in anxiety-to-eat for HED foods and that this heterogeneity is not captured by current diagnostic or clinical measures. Anxiety-to-eat may represent a distinct clinical construct not reflected in standard admission assessments and may warrant incorporation into treatment monitoring.

P139

Circadian Gating Of Vagal Signaling Drives Day-Night Differences In Glucose-Stimulated Insulin SecretionRebeca Mendez-Hernandez^{1,2}, Gabriel Tofani^{1,2}, Mingxin Yang^{1,2}, Lauren Woodie^{2,3}, Mitchell Lazar², Guillaume de Lartigue^{1,2}¹Monell Chemical Senses Center, Philadelphia, PA, United States, ²University of Pennsylvania, Philadelphia, PA, United States, ³George Washington University, Washington, DC, United States

Physiological responses to feeding, including glucose metabolism, exhibit circadian rhythms. In nocturnal rodents, higher glucose tolerance coincides with the peak of food intake at the onset of the active phase, but the peripheral circuits that regulate these rhythms remain unclear. We hypothesized that vagal sensory neurons in the nodose ganglia (NG) exhibit circadian-gated responses to glucose, promoting greater glucose tolerance during the active phase. Methods: We assessed vagal glucose responses, glucose tolerance, and insulin secretion in the resting and active phases in male mice. Results: Using live calcium imaging (n=5/time) and Fos-TRAP labeling (n=7/group), we found that glucose activates NG neurons and the dorsovaginal complex more strongly during the active than the resting phase. Deleting the clock gene *Bmal1* in the NG abolished day-night differences in glucose tolerance by selectively reducing active-phase insulin secretion, suggesting that the local vagal clock is required for circadian glucose control (n=6/group). Ablation of CART neurons (n=6/group) impaired circadian glucose tolerance and insulin secretion, whereas selective re-expression of CART in the NG of global CART knockout mice (n=6/group) rescued both, indicating that CART signaling in the NG was necessary and sufficient for circadian glucose tolerance. Finally, one week of high-fat diet (n=6/group) abolished day-night differences in glucose tolerance, indicating that this vagal mechanism is rapidly disrupted by obesogenic feeding. Conclusion: Vagal sensory neurons act as a peripheral circadian gate for glucose-stimulated insulin secretion through a CART-dependent mechanism. Disruption of this pathway by high-fat diet may represent an early neural mechanism contributing to metabolic dysfunction

P141

Modulation Of Dopamine Responses To Water During Progressive Rehydration

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Water deprivation drives water consumption, in part, by recruiting phasic mesolimbic dopamine responses to water and its cues. As animals consume water, central signals of dehydration quiesce. It remains unknown whether the dopamine response to water is diminished as animals rehydrate. Here, we tested how trial-by-trial rehydration shapes phasic dopamine responses to water. We expressed GRAB_DA3m and implanted a fiber optic in the nucleus accumbens of rats to record dopamine signaling using *in vivo* fiber photometry. Rats were additionally implanted with an intraoral catheter. After recovery, rats received 50 (5s, 200 μ L/trial or 10s, 400 μ L/trial) intraoral infusions of water under ad libitum access to water (ADLIB) or 24h water deprived (DEP), counterbalanced. Intraoral infusions evoked significantly more dopamine release in DEP versus ADLIB sessions. In DEP sessions, there was a significant negative slope in dopamine responses as a function of trial. Moreover, dopamine responses in RES rats decreased twice as fast in sessions with 10s trials relative to those with 5s trials. Rats react to intraoral infusions with stereotypical behavioral responses. We captured the behavioral reactivity of rats on each trial using DeepLabCut and found a close correlation between behavioral reactivity and dopamine responses. Ongoing work includes increasing groups sizes to examine sex differences. The data supports dopamine tracking the dynamic value of water during across physiological state. Dehydration amplifies initial dopamine signaling to water and the rate of rehydration modulates the decline in dopamine as homeostasis is restored. Continuous, state-dependent updating of mesolimbic dopamine during across physiological state, in turn, influences subsequent behavioral reactivity.

P143

Sex Maturation And Bmi Differences In Neuromelanin-Sensitive Mri Among AdolescentsAfroditi Papantoni¹, Camille A. Diamond², Elianna Paninos², Jessica H. Liu^{1,2}, Elayna R. Seago¹, Kyle S. Burger¹¹Monell Chemical Senses Center, Philadelphia, PA, United States, ²University of North Carolina at Chapel Hill, Chapel Hill, NC, United States

Prior studies point to a complex relationship between dopamine (DA) and adiposity, reporting both positive and negative associations across dopaminergic brain pathways and varied levels of body weight. Recently, non-invasive imaging methods for measuring DA in the human brain have been developed, with neuromelanin-sensitive MRI (nmMRI) being used as a validated proxy for midbrain DA metabolism. Our previous work using nmMRI showed evidence of a negative quadratic relationship between DA metabolism and BMI, such as at lower BMI levels, DA was positively related to BMI, but at high BMI levels, DA had an inverse relation with BMI. Here, we used linear regression to test whether this association can be replicated in a sample of healthy-weight adolescents.

Initial results from 43 adolescents (60% female, age=15 $\pm$ 1y, BMI=20.9 $\pm$ 2.6kg/m²) who completed a nmMRI scan show a weak positive relationship between DA metabolism in substantia nigra pars compacta (SNc) and BMI (β =0.271, p=0.063). Interestingly, biological sex was associated with significantly different DA metabolism in the SNc, with females having higher signal than males (β =1.635, p=0.005). We also observed that 69% of females vs. 0% of males had reached self-reported post pubertal period. Animal work has shown that maturation of DA neurotransmission can be impacted during adolescence by sex hormones, with these hormones exerting some of their effects through changes in midbrain DA synthesis. Adolescent hormones could have different actions on DA in males and females, distinct from those in adults. Although our results are preliminary, we report a modest replication of our previous BMI findings in adults and a new association between DA metabolism and sex maturation in the developing human brain.

P145

A Gliotransmitter Target For Metabolic Disease: Octadecaneuropeptide Alters Systemic Nutrient Utilization And Amino Acid MetabolismDestiny Regalia¹, Michaela Murphy¹, Matt Morris², Caroline Geisler¹¹University of Kentucky, Lexington, KY, United States, ²University of Kansas, Lawrence, KS, United States

Octadecaneuropeptide (ODN) is a post-prandially recruited gliotransmitter highly expressed in energy balance centers including the hypothalamus and dorsal vagal complex. We previously demonstrated that targeting central or peripheral ODN signaling improves glycemic control and reduces body weight without nausea/emesis, making it an attractive target for metabolic disease. However, the systemic metabolic impact of ODN treatment remains poorly defined. We first identified that ODN regulates whole-body fuel usage assessed by respiratory quotient. Low-fat diet (LFD) and high-fat diet fed mice (n=8/diet/sex) demonstrated preferential fat utilization in the first two hours after intraperitoneal (IP) ODN treatment. Subsequently, ODN-treated mice only on LFD switched to burn more carbohydrates than controls. To understand if this shift in nutrient oxidation could be attributed to changes in cellular metabolic activity at peripheral tissues directly or through indirect action via the brain, we employed mitochondrial bioenergetics and metabolomics 1-hour post-intracerebroventricular (ICV) or IP treatment of ODN or vehicle in lean mice (n=3/treatment/sex). IP or ICV administered ODN did not alter mitochondrial respiration in brain, muscle, liver, or white adipose tissue of either sex. Metabolomics of medulla and muscle tissue revealed an influence of IP and ICV ODN on steroidogenesis, ether lipid metabolism, as well as histidine, beta-alanine, phenylalanine, and tyrosine metabolism. These data suggest that changes in oxidative respiration may not mediate ODN's effects on systemic nutrient utilization, but amino acid metabolism may be at play. This work helps pinpoint the mechanisms underlying ODN's metabolic regulation to further inform ODN analog treatment for metabolic disease.

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A Microstructural Analysis Of The Control Of Saline Ingestion In Male And Female Rats

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Lick microstructure analysis is a powerful tool used to analyze patterns of fluid and liquid food intake. This approach can provide insight about the mechanisms underlying observed changes in ingestion. Foundational work demonstrated that changes in the number of drinking bursts (at least 2 licks with an inter lick interval of <1s) reflect changes in negative feedback from post-oral sites related to satiety, whereas the average size of those bursts reflects changes in orosensory or hedonic value of the substance being consumed. These conclusions, however, were drawn from studies primarily using sucrose. While follow-up studies have examined the lick microstructure associated with water and saline intake, it is still unclear if the interpretation that changes in burst size being related to the hedonic value of the solution can be extended to saline. We tested the hypothesis that dehydrated rats would show a concentration dependent decrease in saline intake which would be mediated by reduced burst size. Twelve rats (6/sex) underwent 24-h water deprivation, followed by access to 0%, 1%, 2%, or 3% saline. Intake and licks were recorded for 1 h. This was repeated once a week for four weeks until all rats had access to all solutions. As expected, dose-related decreases in intake were observed (p <0.05). This reduction was mediated by decreased burst size (p <0.05), with no reduction in burst number (p = n.s.). In addition, males consumed more saline than females and had larger burst sizes than females (p <0.05). This finding supports the hypothesis that orosensory responsiveness plays a central role in the control of hypertonic saline and extends this work by demonstrating changes in burst size related to saline concentration.

P149

Central Relaxin-3/Rxfrp3 Signaling Potently Drives Orexigenic Behaviors And Attenuates Cisplatin-Induced Anorexia And Body Weight Loss

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The relaxin-3 system has been strongly implicated in having a role in regulating energy balance. Relaxin-3 producing neurons are found in the nucleus incertus (NI) of the brainstem and its receptor, relaxin family peptide receptor 3 (RXFP3), is widely distributed throughout the brain. Central administration of relaxin-3 potently increases food intake in rodents, while central RXFP3 antagonism blocks this effect. These findings suggest that the relaxin-3 system regulates energy balance by modulating feeding behavior, although its underlying neurobiological and physiological mechanisms remain to be determined. Here we characterize mechanisms by which relaxin-3 promotes food intake and food motivated behaviors. Central and systemic administration of relaxin-3 potently drove high-fat diet intake via increasing meal size in obese rats. Furthermore, we generated RXFP3 fl/fl Syn-Cre+ mice, which have RXFP3 knocked out neuronally, and shown that neuronal RXFP3 signaling is required for the orexigenic effects of relaxin-3. In addition, central relaxin-3 augmented food motivation for sucrose in a progressive-ratio task and hyperphagia in a binge-like eating model. We then evaluated the therapeutic potential of relaxin-3 to drive food intake in rats with cancer cachexia, a disorder characterized by metabolic disturbances, anorexia, and body weight loss, of which there are currently no effective therapeutics available. Astonishingly, pretreatment of central relaxin-3 attenuated cisplatin-induced anorexia and body weight loss. Overall, our study characterizes the neurobiological and physiological mechanisms by which the relaxin-3 system drives feeding and food-motivated behaviors and highlights its potential as a therapy for cancer cachexia and other metabolic disorders.

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Central Amygdala Astrocytes Have Calcium Elevations During Food Consumption But Not In Response To Reward-Predictive Cues

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Feeding is a complex behavior that requires the integration of external sensory cues with internal physiological states to guide goal-directed actions. The central amygdala (CeA) serves as a critical hub for reward processing, affective valence, and the regulation of feeding. Prior work has shown that dopamine is released during feeding, but this work has largely focused on neuronal populations. While astrocytes are increasingly recognized as modulators of neuronal network activity, their role in feeding-related behaviors remains poorly understood. Previous studies indicate that astrocytes actively regulate signaling transmission of the local neuronal network in the CeA. We hypothesize that CeA astrocytes respond to dopamine in this area and contribute to the modulation of feeding behavior. To test this, we performed calcium biosensor imaging via 2-photon microscopy on ex vivo brain slices from five mice, confirming that astrocytes directly respond to dopamine independently of neuronal activity. Then, using fiber photometry to record calcium biosensor dynamics, we monitored astrocytic calcium activity in the CeA of five mice engaged in Pavlovian feeding tasks. This revealed that astrocytic activity is modulated during ingestion, independent of internal state, and does not respond to reward-predictive cues. Moreover, astrocytic calcium dynamics track consummatory actions and appear insensitive to the identity or sensory properties of the ingested tastant. Collectively, these results suggest that CeA astrocytes directly detect dopamine and show elevated calcium in response. Furthermore, they support a role for astrocytes in CeA processing during consummatory behavior, positioning them as potential contributors to the neural mechanisms underlying feeding regulation.

P153

Role Of The Bed Nucleus Of The Stria Terminalis In Vulnerability And Resilience To Activity-Based Anorexia

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Activity-based anorexia (ABA) is a widely used animal model that combines restricted access to food with unlimited access to a running wheel. Similar to humans with anorexia nervosa, mice that are vulnerable to ABA increase voluntary exercise and fail to eat enough during food availability to compensate for energy expenditure, leading to life-threatening weight loss. In contrast, ABA resilient mice exhibit an adaptive increase in food intake and reduction in wheel running, leading to weight stabilization (Beeler et al., 2021). However, circuit-level changes mediating these two phenotypes have not been identified. Here, we show that exposure to acute restraint stress increases the proportion of mice that are ABA vulnerable (control: 47% vs. stress: 80%), implicating a role for stress-sensitive brain regions in the underlying pathophysiology. We are currently evaluating effects of ABA on neural activity in the bed nucleus of the stria terminalis (BNST), a brain region known to regulate stress response. Local field potentials (LFP) were recorded from the BNST in awake female mice (n=8) while they were inside a familiar chamber both before and after ABA. Raw LFP signals were filtered for both theta (3-7 Hz) and gamma (20-55 Hz) oscillations. Preliminary analyses (n=3) indicate that ABA vulnerability is associated with increases in BNST theta power and decreases in gamma power, reflecting changes in local network physiology. In ongoing analyses, we are characterizing oscillations in resilient mice and assessing synchrony between the BNST and the nucleus accumbens, a key node of the brain's reward circuitry. This work will reveal neurophysiological signatures of vulnerability and resilience to ABA, providing much needed insight into mechanisms mediating anorexia nervosa.

P155

High-Fat-Type Gastrointestinal Microbiota Transfer Modulates Fentanyl Seeking In Mice

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Rewarding stimuli release dopamine (DA) from the ventral tegmental area (VTA) to the nucleus accumbens (NAc). Germ-free rodent colonization with GI content from high-fat (HF) diet animals leads to a feeding-driven DA release deficit associated with a compensatory intake increase. Here, we aim to determine if an HF-type microbiota also alters the rewarding value of fentanyl, as its consumption triggers DA release in the NAc and deficits in dopaminergic signaling are linked to opioid relapse. We manipulated male and female mice microbiota by exposing them to either HF or chow-fed animal feces (ConvHF or ConvChow), then expose them to a fentanyl conditioned place preference protocol. 16S sequencing, from fecal samples prior drug exposure, revealed that ConvHF microbiome were different from ConvChow, yet also different from HF donors. ConvHF did not develop a fentanyl-paired context preference while ConvChow did, suggesting a dysregulation in reward response in ConvHF. Fentanyl preference was negatively correlated with the abundances of some *Lachnospiraceae* species, which were enriched in the males ConvHF compared to males ConvChow. Separately we assessed fentanyl self-administration in ConvHF and ConvChow males. In this paradigm, mice are allowed to self-infuse fentanyl by nose-poking. Consistent with our previous results, ConvHF mice tend to self-administer less fentanyl than the controls on self-administration 5,6 and 8-12 (p values<0.01). We concluded from this data that the transfer resulted in distinct gut microbiotas in the Conv groups; Conventionalization with a HF-type microbiota appears to reduce fentanyl seeking in both paradigms tested; and some *Lachnospiraceae spp.* may have the capacity to alter reward behaviours.

Therapeutic Potential Of Time-Restricted Feeding In A Mouse Model Of Triple-Negative Breast Cancer

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Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death among women. Triple-negative breast cancer (TNBC), the most aggressive subtype, has limited treatment options. Obesity exacerbates, and 30% calorie restriction improves outcomes in mouse models of TNBC, but this extreme calorie restriction is not easily achievable in free-living humans. Time-restricted feeding (TRF), in which the daily eating window is restricted to 8 hours, improves outcomes in TNBC, but whether this is due to reduced calorie intake, fat loss, or temporal feeding is unknown. Therefore, we hypothesized that 8-hour TRF improvements in TNBC outcomes would be attributable to reduced caloric intake. Female C57BL/6 mice (n = 64) were fed a high-fat, high-sugar (HFHS) diet for 9 weeks to induce obesity. E0771 TNBC cells (0.5×10^6) were then injected into the 4th mammary fat pad. Mice were divided into four groups (n = 16 per group): ad libitum chow, ad libitum HFHS, TRF HFHS, and pair-fed (PF) HFHS, whose caloric intake was matched to the TRF group. Survivorship data were analyzed using Logrank analyses; all other data were analyzed using one- or two-way ANOVAs with Holm-Sidak post hoc analyses (P < .05 considered significant). As expected, ad libitum HFHS-fed animals had greater tumor weights compared with other groups (P = .0400). However, contrary to prior reports, TRF did not reduce calorie intake, induce weight loss, or decrease adiposity in HFHS-fed mice. We further saw no improvement in tumor volume or increased survival. These data suggest that TRF per se may not confer any benefit for TNBC outcomes when weight loss is not achieved.

Blunting Starch Digestion Impairs Metabolic Flexibility In Mice

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Dietary carbohydrate digestion plays a vital role in energy balance and metabolic health, with dysregulation contributing to conditions such as diabetes and obesity. A key component of metabolic health is metabolic flexibility, the ability to shift between carbohydrate and fat oxidation in response to substrate availability. Understanding how carbohydrate digestion and its enzymatic regulation influence substrate use may provide insights into metabolic dysfunction. We hypothesized that reduced starch digestion impairs metabolic flexibility by limiting carbohydrate oxidation and altering energy use. Thus, we examined the effects of impaired starch digestion on metabolic flexibility in maltase-glucoamylase knockout (Mgam KO; ablation of the gene for a starch-digesting glucosidase enzyme) and wild-type (WT) Sv/129 mice (N=16). WT and Mgam KO mice were fed diets containing raw corn starch (53% w/w) with or without acarbose (0.5 g/kg diet) to further blunt starch digestibility. Indirect calorimetry was conducted across two days, and a metabolic flexibility factor (MFF) was derived from RER values. Acarbose supplementation reduced carbohydrate oxidation across genotypes, resulting in lower MFF values, suggesting that reduced starch availability impairs metabolic flexibility. This effect was more pronounced in WT mice. Acarbose exposure on day 1, but not on day 2, accentuated genotype-dependent differences (p < 0.05), indicating potential gut microbial adaptation over time. Acarbose also lowered energy expenditure across genotypes (p < 0.05), suggesting a shift in substrate fate toward fermentation with reduced host energy yield. Overall, these findings suggest that starch digestion and its inhibition alter substrate oxidation, energy expenditure, and metabolic flexibility.

Sex-Dependent Effects Of Perinatal Bisphenol A Exposure On Body Composition And Metabolic Health In Offspring Mice

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Bisphenol A (BPA), a common component of consumer products, is associated with altered metabolic outcomes. In rodents, offspring of BPA-exposed dams show accelerated growth, increased fat mass, and impaired glucose tolerance in a dose- and sex-dependent manner. While BPA combined with a high-fat diet (HFD) worsens metabolic impairments in adult parent males, its effects in offspring remain controversial. We hypothesized that BPA-exposed offspring would exhibit worsened metabolic health, particularly when fed an HFD. To test this, fifty-five CD-1 offspring mice (29 BPA-exposed, 26 controls; 3 weeks old at baseline) were studied for 24 weeks with ad libitum access to a HFD or a control high-carbohydrate diet (HCD). Body weight (BW), body composition, and body length (BL) were assessed longitudinally. Food intake (FI), glucose tolerance (area under the curve, AUC), total energy expenditure (TEE), and locomotion were also measured. Mixed-effects models and t-tests were used for statistical analyses. BPA increased BW in females but not males, with earlier and stronger effects under

HFD ($p < 0.001$). This increase was not explained by adiposity, as fat mass and adiposity index were unchanged ($p > 0.05$). Instead, BPA increased lean mass (LM) in females from ~10 weeks onward. Consistently, BPA-exposed females showed increased BL ($p = 0.00064$), with no differences in males. FI, glucose tolerance, TEE, and locomotion were not affected by BPA ($p > 0.13$), although males showed higher AUC than females ($p = 0.00014$). Overall, perinatal BPA exposure increases BW in a sex-dependent manner, driven by increased LM and BL rather than adiposity. Studies are underway to assess whether increased LM and BL in females reflect skeletal muscle hypertrophy, including changes in myofiber diameter and muscle strength.

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Involvement Of Orexin And Light Environment In The Estrogen-Induced Hypophagia Through Circadian Feeding Regulation In Ovariectomized Rats

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Estrogen replacement in ovariectomized rats reduces food intake, particularly during the light phase. In the present study, we first examined the involvement of orexin A in this estrogenic effect. Estradiol (E2) replacement decreased food intake and attenuated activation of orexin A neurons in the perifornical/lateral hypothalamic area in response to insulin-induced hypoglycemia and 2-deoxy-D-glucose-induced glucoprivation, specifically during the light phase. We also found that exposure to a dark environment during the light phase (dark/dark environment) abolished the estrogen-induced attenuation of food intake and the enhancement of c-Fos expression in the suprachiasmatic nucleus (SCN) during the subjective day. Estrogen replacement increased non-REM sleep duration and decreased wakefulness during the light phase, and enhanced sleep induced by light exposure during the dark phase. These findings indicate that estrogen reduces food intake during the light phase, at least in part, by suppressing orexin neuron activity in a light-dependent manner. Light exposure during the light phase is required for the estrogen-induced hypophagia, and estrogen enhances response to light. In addition, adjustment of the feeding schedule diminished hyperphagia and excessive body weight gain induced by estrogen deficiency. Estrogen effectively attenuates food intake and weight gain by modulating the circadian regulation of feeding behavior through potentiated light-induced attenuation of feeding.

10:00 - 12:00 PM	Millennium Hall
Presidential Symposium	

Chair(s): Kathleen Keller

10:00

From (Controlled) Plate To Paradigm: Honoring A Pioneer Of Portion Size And Energy Density Research

Jennifer O. Fisher

Temple University, Philadelphia, PA, United States

This talk will reflect on the scientific contributions and legacy of Barbara J. Rolls, whose research established portion size and energy density as fundamental determinants of food and energy intake in both children and adults. Drawing on my experiences as a graduate student at Penn State, I will highlight the culture of inquiry and methodological rigor that Barbara fostered, which has shaped my approach to science, as well as that of many others under her tutelage. I will describe how her research on portion size and energy density has shaped key concepts about the regulation of intake and stimulated subsequent work in pediatric populations, including my own. Finally, I will discuss how this evidence has been translated into policy-relevant implications, underscoring the substantial public health impact of her contributions. Central to Barbara's legacy is a commitment to conceptual clarity and rigorous methodology, reflected in the elegant design of her controlled feeding studies and her persistent effort to understand eating behavior from multiple perspectives. This influence endures not only in the body of evidence she produced, but also in the many investigators whose approaches to studying eating behavior remain grounded in her work.

10:30

Shaping The Next Generation: The Impact Of Barbara Rolls's Mentorship On The Field Of Ingestive Behavior

Paige Cunningham

Cornell University, Ithaca, NY, United States

Over a highly impactful career spanning decades, Barbara Rolls has left a giant footprint and proved to be a true luminary in the field of ingestive behavior. Beyond her own work, through her dedication to mentorship Barbara has and continues to shape the next generation of scientists. As her last graduate student, Barbara's mentorship echoes throughout my work and career. Our mechanistic investigation of sensory-specific satiety and hedonic determinants of meal intake contributed to our discovery of switching (alternations between meal components) as a behavior that is significantly associated with food intake in adults and children. Our investigation of the combined effects of variety and portion size highlights the need to consider how properties of food known to influence consumption can work together to drive greater energy intake than either property alone. And together, we developed The Satiation Framework, which moves beyond a focus on physiological fullness to consider satiation as a series of dynamic processes that drive meal termination. This framework informs my multidisciplinary approach to understanding determinants of energy intake at meals. Overall, Barbara's mentorship has influenced not only the research questions that I hope to pursue over the course of my career, but also the way I approach science as a whole – with rigor, with intentionality, and with consideration of real-world implications and how our work can meaningfully benefit human health. So, while I am Barbara's last graduate student, I see this not as an end of an era but as a start of the next generation, still very much shaped by the remarkable mentorship of Barbara Rolls.

11:00

High Volume, High Impact: The Barbara Rolls Effect

Alexandria B Hast

The Campbell's Company, Camden, NJ, United States

Dr. Barbara Rolls has dedicated her career to understanding the fundamental drivers of food intake, producing a body of work on energy density, portion size, and dietary composition that is among the most cited and applied in nutritional science. That scientific legacy extends well beyond publications; it has shaped the careers of an entire generation of researchers now working across academia, government, and industry. Graduate training in the Rolls laboratory is defined by intellectual rigor and careful experimental design. These core competencies translate directly into high-impact careers, including in the food industry, where evidence-based thinking, regulatory fluency, and the ability to connect nutrition science to consumer behavior are increasingly in demand. Effective mentorship develops scientists who can operate at the boundary between discovery and application; and, Barbara Rolls has exemplified this role for decades.

11:30

Translating Science To Improve Health: Using Research To Support Evidence-Based Public Health Nutrition Decision-Making

Julie Obbagy

USDA, Medfield, MA, United States

Barbara Rolls' mentorship directly impacted my decision to pursue a career in the Federal government translating science to improve health. My career involves developing, advancing, and applying methods to conduct systematic reviews and other evidence synthesis projects that examine the complex interplay between diet and health. The values required of gold standard evidence synthesis processes - identification of high-priority research questions, scientific rigor and transparency, management of biases and conflicts of interest, diversity of expertise and collaboration, and effective science communication - are all values that were central to my training experience with Barbara Rolls. Systematic reviews that are high-quality and trustworthy are critical for end users who use their findings to make evidence-based decisions that have real-world public health impact. A recent systematic review that examined the relationship between portion

size and energy intake will be described to demonstrate how research is used to support evidence-based public health nutrition decision-making - and to illustrate the strength of Barbara Rolls' research program.

Oral Session 1: Oh Behave! Understanding Ingestive Behavior

Chair(s): Jennifer Temple

12:15

A Double-Blind Study Of Olfactory/Sniff Training With A Randomized Blank Control GroupRichard L. Doty¹, Crystal Wylie^{1,3}, Ronald Devere², Vince Grosso³, Shima Moein³, Marco Fornazieri⁴¹University of Pennsylvania, Philadelphia, PA, United States, ²Taste and Smell Disorders Clinic, Austin, TX, United States, ³Sensonics International, Haddon Heights, NJ, United States, ⁴Universidade Estadual de Londrina, Londrina, Brazil

Objectives: Persons with smell loss reportedly benefit “olfactory training” (OT). However, most OT studies ignore drop-out rates, lack double-blinding, and do not employ randomly assigned contemporaneous control groups to account for expectation, practice effects, regression to the mean, and spontaneous improvement. We addressed these shortcomings in a double-blind multi-center study, labelling the research “sniff training” to facilitate compliance. **Methods:** Of 134 smell-deficient patients we contacted, 96 agreed to participate. 27% did not complete the 4-month-long training period, resulting in a final study group of 70. The patients were randomly assigned to three 10-stimulus exposure groups: unlabeled odorants; labeled odorants; and odorless blanks. The UPSIT® was administered before and after the training period; 35 also received a smell threshold test. General linear models, $\hat{A}^2$, and other statistical analyses were employed. **Results:** Although 64% improved on the UPSIT®, with 26% experiencing clinically meaningful improvement (i.e., ≥ 4 points), the three odor exposure groups did not differ in terms of such improvement. A 6.2% improvement in UPSIT® scores occurred independent of exposure group ($p=0.003$). A trend in improved threshold scores independent of exposure group was also evident ($p=0.078$). **Conclusion:** We found in a double-blind placebo-controlled study that OT with a blank produced the same degree of improvement over a 4-month training period as OT with olfactory stimuli. Confirmation from other similarly designed studies is clearly needed.

12:30

Momentary Withdrawal Symptoms Predict Ultra-Processed Food Intake During Dietary Reduction

Erica LaFata

Oregon Research Institute, Springfield, OR, United States

Rationale: Ultra-processed foods (UPFs) may engage addiction-like processes that disrupt ingestive control, yet prospective evidence on withdrawal-driven eating dynamics is limited. **Hypothesis:** Reducing UPFs without caloric restriction will elicit withdrawal symptoms that predict momentary lapses in dietary control. **Species:** Humans **Sample:** Adults ($N=18$; 83.3% female; $M_{age}=51.33$; ecological momentary assessment (EMA) data available for $n=17$) **Methods:** Participants completed a 3-day baseline followed by 14 days of UPF reduction while maintaining caloric intake. EMA repeatedly measured withdrawal symptoms (modified ProWS; 7–49 range), urges, and UPF intake ($M=47.1$ surveys per participant over the study period). Multilevel models examined within-person predictors of subsequent intake. **Results:** Withdrawal symptoms were observed in the low-to-mid range ($M=17.29$), consistent with real-time assessment of acute dietary change. Higher withdrawal symptoms predicted increased likelihood of UPF intake at the next timepoint ($ps<.01$), particularly mood-related symptoms (irritability, anxiety, mood swings; $ps<.001$). Urges also predicted subsequent UPF intake ($p<.01$). UPF intake, in turn, predicted subsequent increases in withdrawal symptoms ($p<.001$), indicating a bidirectional process. UPF consumption occurred in 23.0% of EMA reports despite reduction instructions. **Conclusions:** Prospective, real-time data support the presence of withdrawal-like symptoms during UPF reduction and identify negative affect as a key mechanism linking withdrawal to intake. Findings extend prior retrospective work by demonstrating dynamic, within-person associations in daily life and suggest that targeting withdrawal may improve dietary adherence.

12:45

Screen Time Predicts Eating In The Absence Of Hunger In Preschoolers: Attentional Bias To Food As A Candidate Mechanism (Elsevier Appetite New Investigator Travel Awardee)Yashaswini Rajendra Bhat¹, John Brand², Diane Gilbert-Diamond², Jennifer A. Emond¹¹Dept of Biomedical Data Science, Geisel School of Medicine at Dartmouth College, Hanover, NH, United States, ²Dept of Epidemiology, Geisel School of Medicine at Dartmouth College, Hanover, NH, United States

Behavioral Susceptibility Theory states that appetitive traits interact with environment to shape eating behavior. Screen media is a dominant feature of young children’s environment. Food ad exposure increases children’s intake and is associated with weight status, but whether longer term habitual screen time predicts Eating in the Absence of Hunger (EAH) energy intake is unknown. Eye-tracking measures of food attentional bias are associated with weight in children but have not been examined as a mechanism linking screens to eating. We tested whether habitual screen time predicts EAH energy intake in preschoolers and whether attentional bias mediates this relationship. In 42 children (3–5 y), attentional bias to food vs. toy images was measured via eye-tracking and EAH was assessed via a standard protocol. Parents reported weekly screen time (hr/day) through self-reported survey. Five children did not consume anything during the EAH protocol and were excluded from the analysis. In a linear model adjusting for age, sex, BMI-z, and household income, screen time ($M=1.8$, $SD=1.0$ hr/day) predicted log-transformed EAH; at the sample mean, one additional hr/day was associated with 36 additional kcals ($p=.028$). Screen time was positively

associated with first fixation bias (FF) to food (path a: $\beta=0.39$, $p=.068$), and FF with EAH controlling for screen time (path b: $\beta=0.23$, $p=.24$). The direct effect of screen time on EAH controlling for FF was marginally significant, accounting for 16% of the direct effect (c' : $p=.057$). All coefficients are standardized. Results held adjusting for measured physical activity. These findings identify habitual screen time as an early-life exposure correlated with hedonic eating, with attentional bias to cues as a candidate mechanism.

1:00

Food Parenting As A Predictor Of Child Energy Intake After An Experimentally Manipulated Restrictive Period

Muhammad Jamal Khan¹, Hannah E. Kolpack¹, Lori A. Hatzinger², Jennifer L. Temple^{1,3}, Katherine N. Balantekin^{1,3}

¹Department of Exercise and Nutrition Sciences, School of Public Health and Health Professions, University at Buffalo, Buffalo, NY, United States, ²Department of Population and Public Health Sciences, University of Southern California, Los Angeles, CA, United States, ³Center for Ingestive Behavior, University at Buffalo, Buffalo, NY, United States

Controlling food parenting is often associated with less favorable child eating outcomes, whereas positive food parenting is generally associated with more favorable child eating outcomes. The goal of this study was to see how parent-reported typical food parenting predicted child energy intake at a test meal following 2 weeks of experimentally manipulated parental restriction. At baseline, 91 parent-child dyads (8-11 years old; 53.8% male) had their height/weight measured, and the parent completed the Structure and Control in Parent Feeding questionnaire. Parents were then instructed to restrict their child's access to a frequently consumed preferred snack food (chosen from 7 options) and similar foods for 2 weeks. After 2 weeks, the child was given a test meal that contained 25 foods (including their restricted food), and 3 drinks. Linear regression models were used to examine if aspects of controlling food parenting (restriction and pressure to eat) and positive food parenting (consistent feeding routine and limit exposure) predicted child's total energy intake during the test meal, split by child weight status. In children with overweight/obesity, pressure to eat positively predicted energy intake ($p=0.03$). Whereas in children with healthy weight, limit exposure positively predicted energy intake ($p=0.03$). There were no other significant findings. These findings suggest that the impact of experimentally-manipulated restriction may differ based on the typical food parenting environment and the child's weight status.

1:15

Worth The Work: Influence Of Relative Value And Relative Motivation On Sweet Vs. Fruit Intake And Bmi

Jose Jarquin, Olufisayo Atande-Ogunleye, Susan Carnell

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

Food intake and body weight are the cumulative result of choices between consuming less healthy, higher energy-density [ED] foods (e.g. sweets) or healthy, lower ED foods (e.g. fruits). Such food choices are influenced not only by how much an individual values the food (liking, wanting), but by the varied costs they are willing to incur to obtain it (motivation/effort). We investigated how relative value and motivation for sweets vs. fruits, assessed across a variety of cost types, were associated with habitual diet and BMI. We used data from $n=487$ 17-23y olds (70%F, BMI 15-42.5) on the Food Motivation Battery [FMB], assessing willingness to i) exert low effort (finger taps), ii) exert high effort (jumping jacks), and iii) pay for, hypothetical delivery of a selected sweet and fruit that they liked and sometimes consumed. Individuals completed a screener assessing habitual diet, and reported height and weight. Using sweet-fruit difference scores, we found that: Individuals who valued sweets more were more willing to incur costs of multiple types to obtain them (taps: $\beta=0.46$; jumps: $\beta=0.46$; pay: $\beta=0.34$). Greater effort scores for sweets were associated with higher habitual sweet intake (taps: $\beta=0.10$; jumps: $\beta=0.14$). Greater willingness to pay for sweets was associated with higher BMI ($\beta=0.13$), most strongly for those who valued sweets more (value*pay $\beta=0.10$). A similar interaction was seen for taps ($\beta=0.05$, ns). Real-world food choices and BMI are influenced by not only value but the relative costs individuals are willing to incur to obtain less healthy vs. healthy foods. Understanding how individuals weigh value and costs for different foods could identify cognitive or behavioral intervention points to improve diet and metabolic health.

1:30

Are You A Healthy Eater? Using Brain Responses To Food Cues To Predict Motivation To Consume Healthy Foods

Trinity Cheng, Liuyi Chen, Susan Carnell

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

Motivation to consume healthy foods may better predict an individual's obesity risk than the more universally high motivation to consume less healthy foods. To investigate the neural underpinnings of such motivation, we identified a "healthy eater" phenotype in $n=77$ adolescents ($16.3 \pm 1.27y$; $37M$; $BMIz=0.64 \pm 1.21$), then tested whether brain food cue responses could classify individuals into that group. Principal component analysis [PCA] followed by K-means clustering was applied to wanting, liking, frequency and appetizing ratings for fruits and vegetables [F&V] and high energy-density [ED] foods, ad libitum buffet intake, and % empty calories and % fiber intake from ASA24. Two clusters emerged, representing "healthy" ($n=23$), and "less healthy" ($n=23$) eaters. The healthy group showed higher intake and wanting for F&V, and lower intake and other ratings for high-ED foods. We then ran one-vs-rest RandomForest models using fMRI responses to F&V and high-ED food (vs. non-food) images to classify individuals. Models showed best discrimination for both the healthy ($AUC=0.79$, accuracy=71.3%) and less healthy ($AUC=0.82$, accuracy=71.2%) groups when using the F&V contrast as input. Feature importance analyses indicated these predictions were driven by superior parietal lobule, posterior cingulate, and parietal operculum. Traditional voxel-wise linear regression analyses ($p<.001$, cluster $p<0.05$) revealed that healthy vs. less healthy eaters showed greater caudate and superior frontal gyrus responses to high-ED foods, and reduced cerebellum responses across both high-ED and F&V contrasts, with no clusters surviving FDR. Machine learning methods capturing distributed nonlinear brain responses to food cues provide novel insights into neural substrates underlying motivation to consume healthy foods.

Oral Session 2: Ch-Ch-Ch-Ch-Changes: Interventions & Therapeutics

Chair(s): Will de Lartigue

12:15

Control Of Water Intake By Glp-1 Action In The Anteroventral Third Ventricle RegionSydney A David¹, Johanna L Sirkin², Destiny J Brakey², Matthew J Paul¹, Derek Daniels^{2,3}¹Department of Psychology, State University of New York at Buffalo, Buffalo, NY, United States, ²Department of Biological Sciences, State University of New York at Buffalo, Buffalo, NY, United States, ³Center for Ingestive Behavior Research, State University of New York at Buffalo, Buffalo, NY, United States

The mechanisms controlling fluid and food intakes are intertwined, making it challenging to separate the specific neural and hormonal pathways that control each behavior. For instance, glucagon-like peptide-1 (GLP-1) has a role in the suppression of both food and fluid intakes, without clarity about sites of overlap and nonoverlap. The vasopressin-deficient Brattleboro rat provides a unique model to study the thirst-specific elements of the GLP-1 system. Brattleboro rats are polydipsic, and hyper-responsive to the fluid intake suppression caused by GLP-1 receptor (GLP-1R) agonist treatment, but show a hypophagic response to the treatment that is indistinguishable from that observed in wildtype rats. To better understand the brain regions that differ between Brattleboro rats and their wildtype littermates, we examined Fos- and GLP-1R-immunoreactivity after dehydration with or without subsequent access to water. These analyses revealed several areas with main effects of water access or genotype, but the anteroventral third ventricle (AV3V) region had an interaction effect in both the number of Fos-positive cells and the density of GLP-1R-immunoreactivity. We therefore hypothesized that GLP-1 selectively regulates drinking through specific neural circuits converging on the AV3V, rather than through broad activation of feeding-related pathways. In support of this hypothesis, we found that direct administration of the GLP-1R agonist Exendin-4 into the AV3V robustly reduced drinking without affecting feeding. We also observed a selective suppression of drinking when we chemogenetically excited AV3V-projecting neurons in the caudal brainstem. These findings are consistent with the model that GLP-1-related signals from the hindbrain converge on the AV3V to suppress thirst.

12:30

A Psychobioecological Intervention To Address The Food-Insecurity-Obesity ParadoxNicholas V. Neuwald, McKenna E. Nicholls, Sarah E. Naula, Jennifer L. Temple, Leonard H. Epstein
University at Buffalo, Buffalo, NY, United States

Our lab has proposed a psychobioecological model theorizing food insecurity leads to metabolic and psychological adaptations favoring fat storage and increased preference for energy-dense food. Based on this model, we hypothesized that targeting these adaptations through a metabolically tailored diet and by reducing meal unpredictability would attenuate the mechanisms linking food insecurity with obesity risk. Twelve women (BMI 40.4 ± 8.1) with food insecurity and obesity participated in a 2-month stepped-wedge pilot intervention followed by a 2-month follow-up period, combining meal deliveries and behavioral coaching. Participants received 2-3 ready-to-eat meals per day for 4 nonconsecutive weeks, targeting a 20% daily calorie deficit and follow a high-protein (>30%), low-carbohydrate (<40%), low-glycemic-load diet. Weekly behavioral coaching and biweekly metabolic assessments informed individualized meal tailoring. The study is ongoing, with 5 participants having completed the protocol. Among these participants, mean weight loss was 7.5 ± 4.8 lbs. at post-treatment and 10.8 ± 4.0 lbs. at follow-up. The thermic effect of food increased from 2.9% at baseline to 4.6% post-treatment (+59%) and 9.0% at follow-up (+210.3%). Delay discounting decreased by 24.0% at post-treatment and 12.9% at follow-up relative to baseline. Relative reinforcing efficacy for high-energy-dense food declined 59.0% at post-treatment and 78.1% at follow-up, while perceived stress declined 6.7% and 24.7%, respectively. Preliminary findings suggest this treatment led to sustained behavioral and metabolic improvements which provide support for the psychobioecological model as a framework for addressing the food-insecurity-obesity paradox. Complete data will be available prior to the conference.

12:45

Discovering Prokineticin Receptor 2 Agonists For The Treatment Of Obesity (New Investigator Travel Awardee)Kate R. Bowman^{1,2,3}, Ayushi Mittal^{1,2,3}, Paul Buscaglia^{2,3}, Julien A. Sebag^{2,3,4}¹Department of Molecular Physiology and Biophysics, University of Iowa, Iowa City, IA, United States, ²Department of Pharmacology, University of Michigan, Ann Arbor, MI, United States, ³Caswell Diabetes Institute, University of Michigan, Ann Arbor, MI, United States, ⁴Life Sciences Institute, University of Michigan, Ann Arbor, MI, United States

While the rate of obesity is rising, safe and effective weight-loss medications are limited. GLP1R agonists promote weight loss but their use is accompanied by side effects (nausea, gastrointestinal discomfort, loss of muscle mass). It is therefore urgent to find new therapeutic targets for obesity. Prokineticin 2 (PK2) is an anorexigenic neuropeptide that activates two GPCRs, prokineticin receptors 1 and 2 (PKR1 and 2). PKRs are expressed in multiple brain regions and ICV administration of their agonist PK2 reduces food intake and body weight in diet-induced obese mice (n=5-8). PK2 retains its anorexigenic effect in *PKR1 KO* mice, identifying PKR2 as the mediator of the anorexigenic response (n=18-28). Silencing of PKR2 in amygdala neurons, but not arcuate nucleus neurons, abrogates the anorexigenic effect of PK2 (n=5-6), establishing amygdala PKR2 neurons as required for the inhibition of food intake by PK2. Importantly, unlike GLP1R agonists, we found that PK2 does not induce nausea or aversion. Because PK2 is not tractable as a drug, we developed a high-throughput screening assay to identify small molecule PKR2 agonists and screened 85,000 drug-like compounds. Hits were counter-screened against other GPCRs and PKR1 to eliminate non-specific compounds. Lead compounds with specific agonism for PKR2 were further characterized pharmacologically and tested for *in vivo* efficacy. ICV

injection of compounds in mice resulted in significant inhibition of food intake and bodyweight (n=6-9), thus confirming that small molecule PKR2 agonists are promising candidates for the development of new weight loss drugs. Future work will involve chemical optimization of identified compounds to improve potency, efficacy and bioavailability.

1:00

Pre-Meal Olfactory Nudging Vs. Habituation: Feasibility Randomized Controlled Trial In Women With Overweight/Obesity

Surabhi Bhutani¹, Yao Zhao^{2,3}, Emma Johnson¹, Victoria Esparza^{1,2}, Valentina Parma^{2,3}

¹San Diego State University, San Diego, CA, United States, ²Monell Chemical Senses Center, Philadelphia, PA, United States, ³University of Pennsylvania, Philadelphia, PA, United States

Although olfaction influences food choice, odor-based behavioral strategies are understudied in weight-management research. We hypothesized that brief pre-meal olfactory interventions would be feasible/acceptable in women with overweight/obesity and yield short-term changes in olfactory awareness, cravings, and diet outcomes. In a 2-week pilot RCT feasibility trial (N=45F; age 18-55 years; 60% white), participants were randomized to olfactory nudging (ON; brief exposure to “healthy” banana/strawberry fruit odors), olfactory habituation (OH; 10-min exposure to “unhealthy” banana pudding/strawberry cake odors), or control (10-min no-odor exposure) interventions. Baseline BMI and smell identification did not differ by group. ON was rated as more liked/accepted than OH and control (overall p=0.006; pairwise p=0.04 and p=0.007). Post-intervention, olfactory awareness showed a non significant increase in OH ($\Delta=+2.0\pm 8.4$) vs. ON ($\Delta=-2.1\pm 5.0$) and control ($\Delta=-1.7\pm 8.9$). Although total craving scores did not change, adjusted analyses showed that higher baseline autonomous motivation (control: 5.2 ± 1.1 vs. ON: 6.1 ± 0.9 and OH: 6.1 ± 0.7 ; p=0.02) predicted lower carbohydrate craving at 2 week (b=-5.42, p=0.04). Salt craving decreased marginally across groups (p=0.06). Weight change did not differ across groups. Exploratory dietary patterns were mixed, with directional shifts in OH (lower protein and %protein, higher %carbohydrate) and ON (lower %fat). Our preliminary findings suggest that brief olfactory interventions are feasible and acceptable, particularly ON, and may yield short-term exploratory diet-related signals. More in-depth adjusted and longitudinal analyses will clarify relevance for ingestive behavior.

1:15

Effects Of A Restaurant-Based Intervention On Children’s Meal Selection: A Cluster-Randomized Trial

Stephanie Anzman-Frasca^{1,2}, Juliana Goldsmith¹, Mackenzie Ferrante³, Leonard Epstein^{1,2}, April Gampp⁴, Jess Haines⁵, Lucia Leone^{2,6}, Emily McCray¹, Rocco Paluch¹, Sara Tauriello¹

¹Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, NY, United States, ²Center for Ingestive Behavior Research, Buffalo, NY, United States, ³School of Environmental and Biological Sciences, Rutgers University, New Brunswick, NJ, United States, ⁴Independent Health Foundation, Buffalo, NY, United States, ⁵College of Social and Applied Human Sciences, University of Guelph, Guelph, ON, Canada, ⁶School of Public Health and Health Professions, University at Buffalo, Buffalo, NY, United States

Rationale. Restaurants are regular eating contexts for families, but most children’s meals at restaurants do not meet nutritional recommendations. Regular exposure to nutritious options may promote their acceptance. We tested effects of an intervention designed to promote healthier meal selection among children in restaurants. Methods. Six locations of a quick-service restaurant were randomized to intervention or control. Families with 4-to-8-year-old children (n=236) were randomized based on enrollment location and asked to complete 7 restaurant visits after baseline: 6 during a 2-month intervention period and a post-test visit. Intervention components included placemats promoting 2 healthier kids’ meals, the opportunity to select a toy instead of dessert, and a frequent diner card redeemable for a free kids’ meal after ordering a promoted meal 6 times. The primary outcome was whether a promoted meal was ordered at post-test, tested via Fisher’s test. Other outcomes were calories, saturated fat, sodium, and sugar ordered. Results. The intervention did not affect ordering of promoted bundled meals at post-test, although there were group differences in uptake of individual promoted items (p<.05; 28.4% of intervention group ordered a promoted item vs. 19.5% of controls). The intervention decreased calories, saturated fat, and sodium ordered for children during the study (p<.05, p<.01, and p<.01), with no effect on sugar. Yet there were no significant differences in nutritional characteristics of orders by post-test (e.g., 962.6 vs. 1033.5 calories ordered in intervention vs. control group; p=.07). Conclusion. Results show potential for these strategies to promote healthier orders, but effects dissipated over time, suggesting additional efforts are needed for sustainable impacts.

1:30

Comparing Associations Between Adiposity And Eating Behavior Traits In Individuals With And Without Spinal Cord Injury

Gary J Farkas^{1,2}, Paige M Cunningham³, Mark S Nash^{1,2}, Arthur S Berg⁴, Barbara J Rolls⁵

¹Department of Physical Medicine & Rehabilitation, University of Miami Miller School of Medicine, Miami, FL, United States, ²The Miami Project to Cure Paralysis, University of Miami Miller School of Medicine, Miami, FL, United States, ³Division of Nutritional Sciences, Cornell University, Ithaca, NY, United States, ⁴Department of Public Health Sciences, The Pennsylvania State University College of Medicine, Hershey, PA, United States, ⁵Department of Nutritional Sciences, The Pennsylvania State University, University Park, PA, United States

Spinal cord injury (SCI) is associated with excess adiposity, but how altered body composition relates to trait-level eating behaviors remains unclear. We examined differences in self-reported eating behavior characteristics between men with and without chronic SCI and tested whether body composition accounted for differences between groups. Sixteen men with SCI (age: 42 ± 15 y, BMI: 26 ± 5 kg/m²) and 16 controls (age: 42 ± 14 y, BMI: 26 ± 5 kg/m²) completed a whole-body DXA body composition scan and the Three-Factor Eating and Adult Eating Behavior Questionnaires. An exploratory mediation analysis tested whether

body fat percentage (%BF), visceral fat (VF), and fat-free mass (FFM) explained group differences in eating behavior traits. Despite higher %BF and VF and lower FFM (all $p < 0.05$), SCI participants showed lower disinhibition ($d = -1.14$), food responsiveness ($d = -0.75$), enjoyment of food ($d = -0.86$), and greater satiety responsiveness ($d = 0.80$; all $p \leq 0.037$). The lower food responsiveness in SCI was partially explained by greater %BF, which mediated 57% of the group difference ($p = 0.026$). In contrast, differences in the other eating behavior traits were not mediated by body composition measures, reflecting direct effects of SCI. In individuals without SCI, higher disinhibition, food responsiveness, and enjoyment of food, and lower satiety responsiveness are characteristic of obesity and a higher drive to eat. Paradoxically, we found that despite higher adiposity, individuals with SCI report characteristics consistent with a lower drive to eat. Highlighting the complexity of appetite and adiposity in SCI, our results indicate that changes in body composition and other SCI-related mechanisms may alter eating behaviors in ways inconsistent with those observed in non-SCI populations.

1:45 - 3:00 PM	On Own
Lunch on Own	
3:00 - 4:30 PM	Regency B
Symposium 1: You even eat protein, bro?	

Chair(s): Jamie McCutcheon

3:00

Fgf21 Signals Through Hindbrain Neurons To Alter Food Intake And Energy Expenditure During Dietary Protein Restriction

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

Animals detect and respond to variations in nutrient availability, including reductions in dietary protein availability. Our work has established that the liver-derived metabolic hormone FGF21 is critical for adaptive responses to dietary protein restriction, and that it acts directly within the brain to mediate these effects. However, the precise neural circuit mediating these effects remains undefined. Here, we demonstrate that a discrete population of glutamatergic, *Klb*-expressing neurons in the nucleus of the solitary tract (NTS) mediates FGF21 action during protein restriction. Using a *Klb-Flp* mouse line combined with intersectional genetics, we show that NTS-KLB neurons are directly activated by FGF21. Systematic evaluation of previously implicated regions (SCN, PVN, VMH) reveals these areas are not required for FGF21-mediated responses to protein restriction. In contrast, selective ablation of NTS-KLB neurons prevents metabolic adaptations to protein restriction, including changes in food intake, food choice, and energy expenditure, while their chemogenetic activation is sufficient to drive these responses. These findings establish that NTS-KLB neurons directly respond to FGF21 and coordinate adaptive changes during protein restriction, identifying the neural circuit linking dietary protein sensing to metabolic adaptation.

3:30

Understanding The Logic Of Food Preferences In Sickness And Recovery

ANDREW WANG

4:00

Acute Prefrontal Cortex Response (By Functional Near Infra-Red Spectroscopy, Fnirs) To Ingestion Of Protein And Protein Preloads In Humans: Effects On Satiation Efficacy Rate And Subsequent Acute Intake Of Ultra-Processed Food.

Jennifer A Nasser
Drexel University, Philadelphia, PA, United States

Protein is accepted as the most satiating of all macronutrients as well as the macronutrient promoting the greatest satiety interval. Of current relevance to the US diet is the low level of protein per serving (~2 grams or less/100 kcal serving) contained in most ultra-processed foods (UPF), which make up close to 70% of daily caloric intake. This sparked my interest in the potential for proteins to promote satiation if protein ingestion occurred in close proximity to ingestion of UPF. Additionally, I have had an interest in examining the acute effect of protein ingestion on the prefrontal cortex (PFC) response in adult humans under satiating conditions to probe for potential mechanisms of satiation promotion. For this symposium I will present data from studies of protein ingestion as well as protein preload ingestion effects on subsequent acute intake of UPF with respect to regional activation in the PFC (assess by functional near infra-red spectroscopy, fNIRS) and describe a complementary study of protein ingestion effects in rodents assessed under a common protocol used in our human studies as a means of demonstrating causative mechanisms of satiation promotion. The main working hypothesis that underscores all of the protein-based studies is that acute food intake is less when dorsolateral PFC activation prior to, or during the eating episode is greater than dorsomedial PFC activation. Data accumulated in the human studies and complementary animal study is supportive of this hypothesis.

3:00 - 4:30 PM	Millennium Hall
Oral Session 3: From Milk to Meals: Early Life & Child Eating Behavior	

Chair(s): Paige Cunningham

3:00

Early Ingestive Experience With A High-Fat Diet Alters The Developmental Trajectory Of Vagal Satiation Signaling And Produces Enduring Changes In Appetitive Behavior

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Early-life exposure to energy-dense, high-fat foods is increasingly common, yet how early dietary experience shapes the functional establishment of vagal sensory circuits, the primary pathway through which the gut conveys nutrient information to the brain, remains poorly understood. We hypothesized that early-life high-fat diet (HFD) exposure would alter vagally mediated satiation and appetitive behaviors. Litters of C57BL/6J mice were reared on chow (control) or HFD (HFD^{EARLY}) from birth until weaning (postnatal day [P]0–21), after which all offspring were maintained on chow. Behavioral cohorts (n=8–12/sex/group) were fasted overnight, injected with cholecystikinin (CCK), and presented with HFD at different ages to assess satiation. In control mice, robust CCK-dependent feeding inhibition emerged by P45 and persisted into adulthood. In contrast, HFD^{EARLY} mice displayed consistent, adult-like CCK-dependent inhibition at P35, indicating accelerated maturation of satiation signaling. Although adult satiation responses were similar between groups, durable changes in appetitive reward behaviors were revealed by 2-bottle preference and lick microstructure assays: HFD^{EARLY} females consumed more lipid and exhibited enhanced early-phase lipid licking, consistent with amplified appetitive responding. RNA sequencing of P21 nodose ganglia (n=7–8/group) identified 176 differentially expressed genes in HFD^{EARLY} mice, including genes associated with neuronal excitability and synaptic organization, suggesting candidate mechanisms through which early-life diet alters vagal sensitivity. These findings demonstrate that early-life dietary fat alters the developmental trajectory of vagal circuits and produces enduring, nutrient- and sex-specific changes in ingestive behavior.

3:15 **Inflexible Thinking, Inflexible Eating: Poorer Executive Functioning Is Positively Associated With Food Fussiness During Early And Middle Childhood.**

Rachel Fan, Kyle Hallisky, Kathleen L. Keller

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

Picky eating in childhood is common, but extreme pickiness can lead to nutrient deficiencies, making it crucial for treatment to identify underlying cognitive processes. Executive functioning (EF) deficits could be associated with picky eating, which may partly stem from an inability to generalize foods across categories due to deficits in cognitive flexibility (a component of EF). Thus, we investigated whether poorer EF was associated with greater picky eating during early (ages 4–6y) and middle (ages 7–9y) childhood. Age was tested as a moderator, hypothesizing that the relationship would weaken with age due to a general improvement in EF and reduction of picky eating. A secondary data analysis from two multi-visit cohort studies (n=136; F=66) was conducted. Parents completed the Behavior Rating Inventory of Executive Function (BRIEF2) for assessment of child EF (higher scores = worse EF) and the Child Eating Behavior Questionnaire Food Fussiness (FF) subscale for assessment of picky eating (higher scores = greater FF). Linear regression models (adjusted for parent income and education, child sex and BMI percentile (3.9–99.7), and study) found that poorer general EF was associated with greater FF ($\beta=.35$, $p<.001$). When considering the BRIEF2 subscales, the relationship with greater FF persisted for poorer behavioral regulation ($\beta=.31$, $p<.001$), emotional regulation ($\beta=.24$, $p=.006$), and cognitive regulation ($\beta=.33$, $p<.001$). Worse shifting abilities, or cognitive inflexibility, were also associated with greater FF ($\beta=.28$, $p=.002$). The relationship between EF and FF did not vary by child age ($p=.71$). These results suggest that EF could be a potential mechanistic process that contributes to picky eating across childhood, helping elucidate viable intervention targets.

3:30 **Variety-Seeking When Eating In The Absence Of Hunger As An Obesogenic Eating Behavior In Children**

John W. Long, Barbara J. Rolls, Kathleen L. Keller

Pennsylvania State University, University Park, PA, United States

Modern environments are characterized by abundant food variety but the extent to which children's response to such variety presents a risk for overconsumption and obesity is unclear. We examined whether trying a greater number of foods while eating in the absence of hunger (EAH) was associated with children's energy intake and adiposity, and whether these relations differed by appetitive traits. Children aged 7–9 without obesity completed a year-long study with EAH and body composition measured at baseline (T1; n=100) and follow-up (T2; n=80). At each visit, children consumed a standard meal to satiation followed 15 min later by 9 energy-dense foods (2.2–5.7 kcal/g) to assess EAH. Parents reported children's appetitive traits via the Children's Eating Behavior Questionnaire. Using pooled data across visits, linear mixed models examined whether number of foods tried (≥ 2 g eaten) predicted EAH energy intake and adiposity, and whether these relations were moderated by appetitive traits. Models were adjusted for visit number, sex, age, puberty, education, income, and maternal obesity. Across visits, foods tried predicted EAH energy intake, with each food tried corresponding to an additional 54.6 ± 5.5 kcal consumed ($p<0.0001$). Trying more foods was also associated with higher adiposity, including visceral adipose tissue and fat mass index (all $p<0.05$). Food and satiety responsiveness moderated associations between foods tried and EAH intake (FR: $\beta = 17.7$; SR: $\beta = -28.7$; both $p<0.01$) and visceral adipose tissue (FR: $\beta = 4.3$; SR: $\beta = -6.3$; both $p<0.05$). These findings suggest variety-seeking behaviors in food-rich environments contribute to obesogenic eating, particularly among children with greater food responsiveness and weaker satiety responsiveness.

3:45 **Cancelled - Exposure And Access Drive Intake: A School-Based Produce Intervention Increases Fruit Consumption (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))**

Smadar Hod-Ovadia^{1,2}, Moran Kilzi^{1,2}, Mona Boaz¹, Vered Kaufman-Shriqui^{1,3}

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Rational: Low fruit and vegetable intake is associated with increased chronic disease risk, particularly among low socioeconomic status (SES) populations due to cost and access barriers. School-based food distribution programs may provide a non-stigmatizing mechanism to improve dietary behaviors among families. **Hypothesis:** A combined intervention of rescued produce distribution and nutrition education will improve parental fruit and vegetable consumption. **Species:** Humans (parents of elementary school children) **Number of subjects:** 196 participants **Procedures (methods and statistical analyses):** A 7-month cluster-controlled study in three schools assigned parents to: produce plus education (n=80), produce only (n=66), or control (n=50). Pre- and post-online questionnaires assessed diet and food security. Group differences were tested statistically, and logistic regression examined associations between the number of packages and improved consumption. **Results:** At baseline, 78% of parents consumed fewer than the recommended amounts of fruit and vegetables. Fruit consumption improved significantly in the intervention groups compared with the control group (p=0.028). Among households with worsening food security (8.7% to 14.3%), the combined intervention showed a protective effect on fruit intake (p=0.007). Each additional package increased the likelihood of improved fruit consumption by 6.7% (OR=1.067, 95% CI 1.003–1.135, p=0.04). **Conclusions:** School-based distribution of rescued produce, especially with nutrition education, improves parental fruit intake and may mitigate worsening food insecurity. This scalable, dignity-preserving model integrates food banks and schools to reduce nutritional disparities during rising food costs.

4:00

Food And Game-Time Delay Discounting: Associations With Appetite And Weight In Middle Childhood

Wenxuan Fan¹, Rosa Cano Lorente², Daphne Koinis-Mitchell², Viren D'Sa², Keri Rosch¹, Susan Carnell¹

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Appetitive traits such as food responsiveness [FR] are associated with child weight. Cognitive traits such as delay discounting [DD] – preference for a smaller sooner vs. larger later reward – are also associated with weight, but findings vary with reward type and age. To test an overarching hypothesis that FR and DD play complementary roles in food intake and weight, we assessed in RESONATE (a sub-study of RESONANCE) parent-report FR in 61 7-13y olds (61%M, BMIz 0.39±1.20), along with two experiential measures of DD with high salience in children: a food DD task (5 trials requiring choices between a smaller immediate vs. larger delayed candy reward), and a novel game-time DD task (9 trials requiring choices between shorter immediate vs. longer delayed game access). Children then underwent a post-meal eating in the absence hunger [EAH] test including fruit as well as snacks. Children chose the larger, delayed food reward on 4.08±1.07 trials, and the longer, delayed game access on 58.6±31.0% of trials. EAH intake was 152±131kcal (116±120kcal snacks, 36±50kcal fruit). FR was associated with food DD (r=0.27, p=0.041), but not game DD. Food and game DD were correlated (r=0.29, p=0.024). FR (but not food or game DD) was associated with child BMIz (r=0.29, p=0.026). FR was also associated with greater intake of snacks as a proportion of total intake but only in older children (FR*age p=0.049). Our findings demonstrate that parent-report FR and food DD, and measures of DD in relation to food and game-time, are related within individuals, but in middle childhood only parent-report FR predicts food intake and weight. Future RESONANCE analyses will combine brain and behavior data to test how appetitive and cognitive traits interact to influence intake and weight through development.

4:15

Maternal Prebiotic Supplementation Shapes Offspring Gut Microbiome And Improves Gut-Brain Axis Communication Into Adulthood

Jennifer M. Houston¹, Jillian M. Allen², Julia C. Cook¹, Rachel E. Lippincott², Eden E. Crain², Jung H. Byun², Dulce M. Minaya², Kellie L. Tamashiro³, Claire B. de La Serre¹

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Gut-innervating vagal afferents terminate in the nucleus of the solitary tract (NTS), conveying post-ingestive cues to regulate meal size. Maternal obesity increases risk of metabolic disorders in offspring. Rat pups born to high fat (HF)-fed dams show reduced sensitivity to gut satiety peptides and reduced post-prandial NTS activation associated with increased meal size. HF diet-driven microbiota changes are necessary and sufficient to disrupt gut-brain communication. We hypothesized improving HF-fed dams' microbiota would improve offspring gut-brain signaling. Sprague-Dawley dams were fed a chow, HF, or HF+12% resistant starch (RS) diet during pregnancy and lactation. Chow and HFRS dam microbiome profiles did not significantly differ. At post-natal day 10 (P10), HF offspring were enriched in pro-inflammatory *Bacteroidaceae* compared to chow offspring. HFRS pups were enriched in *Bifidobacteriaceae*, associated with leanness. HF pups displayed reduced Iba1+ and increased Iba1+ staining at the NTS (p<0.05), indicating inflammation-driven vagal withdrawal. Despite chow weaning, gut-brain axis inflammation persisted in adult HF offspring (p<0.01). Adult HF offspring showed reduced CART activation and increased Iba1+ staining in the nodose ganglion, indicating chronic inflammation and altered post-ingestive signaling (p<0.05). HF offspring had increased meal size and failed to reduce intake in response to cholecystokinin (CCK, 1.5µg/mL/kg). Maternal supplementation prevented gut-brain axis inflammation and altered vagal signaling, evidenced by reduced Iba1 and restored CART activation post-ingestion. Maternal HF diet increases pro-inflammatory microbiota and alters vagal structure and function. Maternal RS supplementation can improve gut-brain communication into adulthood.

P102 **Food Insecurity And Emotional Eating: Distinguishing Behavioral And Psychosocial Pathways In First Generation College Students**

Leticia Andrade¹, Jennifer L Temple^{1,2}

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Introduction: Food insecurity is highly prevalent among college students and has been linked to disordered eating, often conceptualized through restriction-binge cycles. However, less is known about whether food insecurity is associated with broader psychosocial processes beyond eating pathology, such as emotional eating and body dissatisfaction. **Methods:** Cross-sectional data from first-generation college students (N = 31) were analyzed. The relationships between food insecurity and emotional eating (Emotional Eating Scale; EES), body dissatisfaction (Body Esteem Scale; BES), and disordered eating (Eating Attitudes Test; EAT; Eating Disorder Examination Questionnaire; EDE-Q) were examined using linear regression models with age, biological sex, and BMI as covariates. **Results:** Food insecurity was significantly associated with EES total score (b = 0.10; p = 0.017), but not with BES, EAT, or EDE-Q scores. Higher BMI was associated with lower scores on BES (b = -0.026; p = 0.009) and higher scores on EDE-Q (b = 0.086; p = 0.023). There was a trend for food insecurity to act as a moderator of the relationship between BMI percentile and EDE-Q score (p = 0.10), but not BMI percentile and BES. **Conclusion:** These findings suggest that food insecurity may be more strongly linked to emotional eating as a coping behavior rather than to broader eating disorder psychopathology or body dissatisfaction in this population. This highlights the importance of distinguishing between behavioral and clinical pathways when examining eating disorder risk in food-insecure college students.

P104 **Chronic Daily Treatment With Semaglutide Leads To Tolerance To The Protective Effect Of Semaglutide On Cue-Induced Fentanyl Seeking And On Body Weight Loss In Rats**

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Glucagon-like peptide-1 receptor agonists (GLP-1RAs) reduce drug seeking in preclinical models, however most studies examine the effect of acute administration despite the likely need for chronic treatment in clinical use. Here, we investigated the effect of chronic semaglutide treatment on fentanyl seeking after abstinence and on food intake, water intake, and body weight. Male Sprague Dawley rats (n=48) self-administered fentanyl (1.85 µg/infusion, FR10, 6 h/day, 14 days) or saline, followed by 14 days of abstinence with daily semaglutide treatment (0.026, 0.056, 0.078 mg/kg, SC). Cue-Induced fentanyl seeking was assessed under extinction conditions. Body weight, food intake, and water intake were monitored throughout. The data were analyzed using repeated measures ANOVA and planned comparisons. Acute semaglutide reduced cue-induced fentanyl seeking, consistent with prior work. In contrast, chronic treatment failed to reduce cue-induced responding at any daily dose, indicating tolerance to the protective effects of semaglutide. Semaglutide initially suppressed body weight gain, but this effect attenuated with repeated dosing, with weight trajectories converging toward those of vehicle-treated controls at later timepoints. These findings indicate that the effects of semaglutide on opioid seeking and energy balance can be mitigated by chronic daily dosing. While this effect may relate to daily dosing with a long-acting GLP-1RA, this work highlights the importance of treatment regimen in determining the efficacy of GLP-1RAs and has implications for their potential chronic use for the treatment of opioid use disorder. This work was supported by UG3 DA030325.

P106 **The Maintenance Gap: Children Maintain Initial Weight Loss More Easily Than Adults**

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Family-based behavioral treatment (FBT) is an evidence-based intervention for familial obesity. FBT provides an ideal format to assess whether children or their parents have an easier time losing and subsequently maintaining weight loss, as they are provided with the same program. To evaluate this question, data from 10 FBT randomized controlled trials were pooled into an individual participant database (IPD) comprised of 470 families. Participants included children ages 6-12 with overweight (> 85th-95th BMI percentile) or obesity (> 95th BMI percentile) as well as their participating parent. The average child showed a reduction in zBMI of 0.41 ± 0.31 at 6 months, with 61.9% achieving a clinically meaningful outcome (zBMI change

P108 **Parent Encouragement Of Weight Loss Negatively Predicted Child Zbmi Change In Younger Children But Not Older Children**

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Research has found that encouragement of weight loss in children is counter-productive, often resulting in increased disordered eating and weight gain. While age has been assessed as a covariate, there is no known study assessing these relationships by age groups. The current study aims to examine relationships between encouragement of weight loss and change in child zBMI and restraint over 1 year in younger (ages 8-9) and older (ages 10-11) children. 104 parent-child dyads participated in a longitudinal study examining child eating behaviors, food parenting, and weight status. Participants had their height/weight measured, parents completed the Parent Encouragement of Child Weight Loss (PEWL) questionnaire, and children completed the Dutch Eating Behavior Questionnaire (DEBQ). Height/weight and DEBQ were assessed at both baseline and 1 year follow-up. Linear regression models were used to examine the relationships between the PEWL score and change in child zBMI and restraint scores (calculated using the DEBQ). Analyses were conducted in the whole sample and split by age groups. PEWL was larger in the older group ($p=.005$) and did not predict change in zBMI or restraint score in the total sample or in the older group ($ps>.269$). PEWL negatively predicted decreased zBMI in the younger group ($p=.045$) but did not predict restraint score change ($p=.800$). These data suggest that PEWL is not a predictor of child-reported restraint, however other appetitive traits should be assessed. Regarding zBMI change, PEWL only predicted change in the younger group, which means intervention efforts at the parent level may be most effective within this age group. Future work should assess how different types of encouragement yield more positive or negative eating and weight outcomes.

P110

Perceived Healthfulness And Ingredient Drivers Of Adolescent Beverage Choice

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Adolescents are frequently exposed to food and beverage marketing online, particularly for energy drinks. While branding is known to influence beverage selection, less is understood about how adolescents perceive beverages based on healthfulness, liking, sugar content, and the presence of specific ingredients including adaptogens, caffeine, protein, and vitamins. Understanding these perceptions may help identify modifiable influences on beverage choice. This study examined how adolescents perceive and prioritize these factors across common beverages. Adolescents aged 13–17 years ($N = 503$) completed an online survey evaluating five beverages: energy drinks, milk, flavored milk, yogurt drinks, and protein drinks. Participants rated perceived healthfulness, liking, and the importance of low/no sugar, caffeine, adaptogens, protein, and vitamins on a 0–10 scale. Due to non-normal distributions, Kruskal–Wallis H tests were used, followed by Dunn's post hoc tests with Bonferroni adjustment ($\alpha = .05$). Significant differences across beverage types were observed for several outcomes ($p < .05$). Milk received the highest ratings for perceived healthfulness, while energy drinks were lowest. Flavored milk received the highest liking ratings. The importance of caffeine and taurine was highest for energy drinks compared to other beverages, whereas protein was rated least important for energy drinks but highly important for milk and yogurt drinks, along with vitamins ($p < .05$). No differences were found for low/no sugar or adaptogens. Adolescents differentiated beverages based on perceived healthfulness and ingredient profiles. These findings suggest ingredient-focused messaging may shape perceptions and may represent a strategy for promoting healthier beverage choices among youth.

P112

Male And Female Mice Use Different Exploration-Exploitation Strategies During Home-Cage Reversal Learning

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Animals must balance exploiting known food sources vs. exploring new alternatives that may yield greater rewards. Here we examined sex differences in explore/exploit strategies in 136 C57BL/6J mice (74M, 62F) using four closed economy tasks with the Feeding Experimentation Device 3 (FED3). First, mice performed a deterministic reversal task over 3 days, in which one nose-poke delivered a food pellet and the other a 10s timeout, switching the active poke every

20 pellets. Male mice showed more efficient foraging, driven by a stronger exploitative strategy (unpaired t-tests, $p=0.001$ for both). Next, the same mice were tested on a fixed-ratio one (FR1) task with no switches for 1 day. Males again showed greater efficiency and win-stay behaviour (unpaired t-tests, $p<0.001$ for both), confirming the sex difference in exploitation also occurred in a non-reversing task. Exploitation improves performance in certain food environments, while exploration can be advantageous under less certain conditions. We therefore hypothesized that the sex difference in exploitation would not result in higher efficiency in probabilistic variant of the reversal task. Consistent with our hypothesis, in a probabilistic (80%/20%) variant of the reversal task, males maintained higher win-stay behaviour (unpaired t-test, $p=0.001$) but no longer showed greater foraging efficiency than females (unpaired t-test, $p=1.0$). Finally, we used a progressive ratio task to quantify motivation for food reward. We detected no sex differences, indicating that the differences in exploitation do not reflect underlying differences in motivation for food. Together, these findings suggest that males are more exploitative than females, which produces more efficient foraging in certain, but not uncertain, environments.

P114 Associations Between Food Cue Responsivity Measures And Loss-Of-Control Eating Episode Frequency And Binge Eating Severity Among Veterans

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Appetitive traits are implicated in binge eating, but the associations between food cue responsivity measures and loss-of-control (LOC) episodes and binge eating severity are unknown. We compared the Food Cue Responsivity Scale (FCRS), a brief composite measure derived from instruments measuring aspects of food cue responsivity, with related measures to characterize associations with LOC frequency and binge severity. Baseline data were analyzed from 129 Veterans in a binge eating/weight loss trial. Included cue/reward measures were the FCRS, Adult Eating Behavior Questionnaire (AEBQ; Food Responsiveness) and the source instruments for the FCRS items: Reward-Based Eating Drive Scale-13 (RED-13), Power of Food Scale (PFS), and Food Craving Questionnaire-Trait (FCQT). LOC episodes and binge severity were assessed with the Eating Disorder Examination and Binge Eating Scale (BES), respectively. Past 3-month LOC episode counts were categorized by estimated weekly frequency ($\leq 3/\text{wk}$; $4-6/\text{wk}$; $\geq 6/\text{wk}$). We fit parallel multivariable models entering one cue/reward measure at a time (z-scored), adjusting for age, sex, baseline BMI, and race/ethnicity. All measures were significantly associated with higher LOC category and BES. For LOC, model fit was best for FCRS and RED-13 (OR=1.84, 1.83; both $p=0.001$), with nearly identical AIC ($\Delta\text{AIC}=0.03$). For BES, fit favored FCQT ($\beta=4.76$, $p<0.001$) and RED-13 ($\beta=4.87$, $p<0.001$; both adj $R^2=0.56$) and FCRS also showed a strong association ($\beta=4.43$, $p<0.001$; adj $R^2=0.46$). Results support food cue/reward responsivity as consistently associated with both LOC frequency and binge severity. They also suggest FCRS may be a feasible low-burden alternative for assessing food cue/reward responsivity

P116 Rethinking Food Parenting Measurement For Adolescents: Parents’ Perspectives On The Comprehensive Feeding Practices Questionnaire (Cfppq)

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The Comprehensive Feeding Practices Questionnaire (CFPQ) is a widely used assessment of food-related parenting practices, developed and validated in 2007 for parents of children and encompassing 12 subscales of behavior. To date, no validated FPP questionnaires exist specific to U.S. samples. This study examined parents’ perspectives on the appropriateness of the CFPQ for assessing FPP of teens. We conducted structured interviews with parents (child 13–17yr) as part of a larger study on adolescent food choices and type 2 diabetes risk. Audio-recorded interviews were completed after parents finished the CFPQ and assessed perceptions of item relevance, repetitiveness, and content gaps. Rapid qualitative analysis was conducted across 34 parent interviews (91% mothers). We found only 35% of parents felt items were relevant to teenage eating behaviors. Irrelevant or problematic topics included parental control, use of food for emotion regulation or reward, monitoring food intake, and availability of unhealthy foods at home. Parents described eating away from teens due to school or employment. Additionally, 38% reported items were repetitive or overemphasized, particularly restriction, control, and snack tracking. Parents were uncomfortable with use of “fat” terminology and felt questions about pressuring teens to eat or feeding when not hungry were developmentally inappropriate. These findings suggest the CFPQ does not adequately capture food-related parenting practices for U.S. adolescents and highlight key areas for adaptation. Developing an adolescent-focused measure that deemphasizes stigmatizing language and parental tracking while incorporating practices relevant to independent eating may better inform family-based dietary interventions for chronic disease prevention.

P118 Efficacy And Safety Of Semaglutide For Obesity And Hyperphagia In Adults With Prader-Willi Syndrome

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Background: Prader-Willi syndrome is a genetic neurodevelopmental disorder with loss of imprinted genes on chromosome 15q11-13 characterized by hyperphagia and early-onset obesity from hypothalamic dysfunction, and learning disability. Management is challenging with strict control of the food

environment needed. While newer glucagon-like peptide-1 receptor agonists, such as semaglutide, have efficacy in non-PWS obesity, there have been few limited case reports in PWS. **Methods:** Retrospective review of adults with PWS and overweight/obesity treated with semaglutide at a specialist UK centre. Outcomes taken from health records included weight, hyperphagia questionnaire for clinical trials (HQ-CT, max 36), glycaemic control and side effects. **Results:** In 12 adults, mean age was 28.3±10.1y, 83% female, mean±SD BMI 46.6±8.2kg/m², 75% type 2 diabetes. Median follow-up was 17.2mo (8.7-33.1), with median dose 2.4mg once weekly (1.0-2.4). Although there was no significant weight loss on semaglutide, there was stabilisation of weight gain prior to treatment over previous 12.4mo (7.6-23.0) (post -3.1±9.9% vs. pre +5.7±5.6%: d -0.72, P=0.037). There was a significant decrease in hyperphagia on semaglutide (n=11, HQ-CT -7.3±6.1, d -1.19, P=0.003), having been stable before treatment, with no change in food environment (Food Safe Zone questionnaire). HbA1c improved in those with elevated baseline levels (n=6, -4.2±4.9%, d -0.74, P=0.13). Mild gastrointestinal side effects were seen in 25% but did not lead to discontinuation. **Conclusion:** In adults with PWS, semaglutide produced weight maintenance, reduced hyperphagia, and improved glycaemic control, with good tolerability. Larger placebo-controlled trials are needed to confirm these findings.

P120

Trajectories Of Protein Intake From Infant Formula And Complementary Foods

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Rationale/Premise: Recent critiques call for reevaluating protein intake recommendations for infants, particularly regarding formula. **Hypothesis:** Protein intakes vary by formula type and the form (free vs bound) of the protein ingested is more important than total intake for later overweight risk. **Species:** Humans **Number of subjects:** 141 **Procedures:** Secondary analyses were conducted on intake data from formula-fed infants who were randomized at 0.5 months to be fed isocaloric formulas that differed in protein content: cow's milk formula (CMF; 2.1 g protein/100 kcal, <1% as free amino acids [FAA]) or extensively protein hydrolyzed formula (EHF; 2.8 g protein/100 kcal, ~50% as FAA). Daily intakes were assessed at 15 time points up to 18.5 months by weighed bottle methods and/or prospective diet records. Foods were categorized into mutually exclusive 'What We Eat in America' categories, and overweight risk was determined. **Results:** For the first year, EHF group had higher protein intakes than CMF group ($p < 0.001$). Formula accounted for more than half of total protein intake in both groups up until 10.5 mos but was no longer a source of protein in the diet at 18.5 mos for all but three. Protein intake from other foods steadily increased from 5.5 mos ($p < 0.001$). At 18.5 mos, the top protein sources were dairy (1.0 ± 0.1 g/kg/d), chicken (0.8 ± 0.1 g/kg/d), and mixed dishes (0.9 ± 0.1 g/kg/d). EHF group had lower risk of overweight at 18.5 mos than CMF (RRR = 0.42, 95% CI: 0.20-0.86, $p = 0.02$) and higher protein intakes were associated with 25% lower relative risk of overweight (RRR = 0.75, 95% CI: 0.64-0.88, $p = 0.001$). **Conclusions:** Formula-fed infants are not a homogenous group. The form, rather than amount, of protein in infant formula may be more important in predicting risks.

P124

Contribution Of Fgf21 And Macronutrient Composition Towards Glp1R Agonist-Induced Weight Loss

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The present study investigates factors influencing weight loss effectiveness of Glucagon-like peptide-1 receptor (Glp1r) agonists. We have shown that liraglutide (lira) promotes greater weight loss in lean mice fed a high-carbohydrate (carb) vs. a low-carb diet, and this depends on liver Fibroblast Growth Factor-21 (FGF21) and neuronal b-klotho (KLB), the FGF21 co-receptor. We tested the hypotheses that: 1) FGF21 contributes to lira weight loss in obese mice fed high fat, high carb (HFHC) diets; 2) carb source (starch vs. sucrose) modulates this; and 3) lira-induced FGF21 targets ventromedial hypothalamus (VMH) KLB to promote weight loss in mice fed HFHC diets. Male control and liver FGF21 knockout (LKO) mice ($N = 9-14$ /gp) and control and VMH KLB knockout (VKO) mice ($N = 12$ /gp) were fed HFHC diets with starch or sucrose as the carb source for 11wks prior to 14d lira treatment and daily weight measurement. In separate experiments, mice were switched to a low-fat, high carb (LFHC) version of each diet 1 day prior to lira treatment. HFHC-fed control and LKO mice lost equivalent weight in response to lira regardless of carb source. However, LKO mice lost less weight in response to lira when switched to LFHC diets prior to lira treatment regardless of carb source ($p < 0.0001$, 2wayANOVA). HFHC-fed VKO mice also lost equivalent weight as controls when treated with lira but were protected from weight loss when switched to LFHC one day prior to lira treatment ($p < 0.0001$, 2wayANOVA). These findings show that lira-induced liver FGF21 and subsequent FGF21 targeting the VMH contribute to weight loss in obese when switched to a low-fat diet prior to treatment. This suggests that dietary carb AND fat content influences Glp1r agonist weight loss and FGF21 contributes to this effect.

P126

Sensory And Metabolic Drivers Of Spatial Memory For Food Location

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Environmental cues guide effective foraging through spatial learning. Foods, particularly sugars, have multiple features that reinforce behavior, including taste and postingestive effects. However, the relative contributions of these features to spatial food memory remain poorly understood. Here, we utilized a reference memory task to determine if taste, calories, and/or a combination of the two reinforce learning about food location in a Barnes maze. Male Sprague Dawley rats were offered access to either 11% sucrose, 0.2% saccharin, or a mixture of 0.2% saccharin and 2% sucrose in a specific hole over four training days. Prior work showed that the saccharin-sucrose mixture elicits a robustly reinforcing oral signal, greater than the more caloric 11% sucrose and the non-nutritive sweetener 0.2% saccharin, but triggers weaker gut feedback than 11% sucrose. All three groups decreased their latency to find the correct (baited) hole across trials, at

comparable rates. Yet, in a probe test, in which the reinforcer was absent, rats trained with sucrose or the saccharin-sucrose mixture displayed a greater proportion of correct investigations, performing above chance levels. Conversely, rats trained with saccharin alone failed to perform above chance. These results suggest that the reinforcing value of food for spatial reference memory arises from both oral and post-ingestive input, such that caloric content can foster learning even when taste is weak, whereas hyperpalatable taste alone may be sufficient despite low caloric yield. Ongoing studies are leveraging site-specific nutrient delivery (oral/gastric) to investigate how hippocampal neurons encode taste versus post-ingestive features of sugar, and how this information supports spatial learning and consummatory behaviors.

P128

Salivary Amylase Alters Taste Driven Behaviors.

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Salivary α -amylase (sAA; encoded by *AMY1*) breaks complex starches into simple sugars in the oral cavity and may shape how complex carbohydrates are sensed and metabolically signaled. However, causality has been difficult to establish because human studies are largely correlational, confounded by *AMY1* copy number variation, and are based on the use of pharmacologic inhibitors such as acarbose, which are not specific to sAA. To study salivary amylase function, we created an Amy1 CRISPR knock-out (KO) mouse that does not produce sAA but still has normal pancreatic amylase expression and function. With this model, we tested if sAA affects taste guided responses to carbohydrates. In brief-access taste tests designed to minimize post oral feedback, wild type (WT) and KO mice showed similar responses to long-chain maltodextrin (DE 16.5-19.5) or any 'sweet' solution tested, but KO mice licked more to a medium-chain maltodextrin solution (DE 13-17, $p = 0.005$), consistent with increased responsiveness to a "starch" taste in the absence of sAA. We then asked whether loss of sAA shifts preferences between maltodextrin and simple sugars. In 24 h two bottle preference tests, WT mice preferred maltodextrins over maltose at low concentrations (p 's < 0.04) but preferred maltose at high concentration (p 's < 0.01). In contrast, KO mice preferred maltose over maltodextrins at both concentrations (p 's < 0.05). Overall, these results suggest that eliminating sAA increases immediate oral responsiveness to maltodextrin, but over longer periods of time, maltodextrin preference is reduced. Hence, sAA appears to influence our initial sensory evaluation of starch as well as the signals that occur post ingestion, that ultimately guide our choices of which carbohydrates to eat.

P130

Ventromedial Hypothalamic Nucleus Subset Can Reverse Diet-Induced Obesity And Diabetes Via Catabolic Events In The Adipose Tissue.

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The Ventromedial hypothalamic nucleus (VMN) contains a mixed population of cells involved in reproductive function, defensive behaviors, and glucose homeostasis, but the mechanisms have only been partially defined. We previously identified a VMN subset that contains pituitary adenylate cyclase activating polypeptide (PACAP, gene: *Adyap1*) which stimulates brown and beige adipose tissue thermogenesis via the preoptic area. However, the potential of targeting these cells on a chronic timeframe has not been established. Therefore, we introduced cre-inducible Kir2.1 and NachBach to chronically shift the probability of firing of these cells in diet-induced obesity. Reducing firing via cre-inducible Kir2.1 in *Adyap1*^{Cre} male and female mice increased weight gain by 50% on a high fat diet for 14 weeks. The results were suggestive of an energy expenditure effect because observed hyperphagia was mild and delayed. Conversely, we introduced cre-inducible NachBach in diet-induced obese and glucose intolerant male and female *Adyap1*^{Cre} mice at thermoneutral conditions (28°C). Increasing the firing of VMN^{PACAP} cells reduced body weight by 20 grams within two weeks. Body weight loss was associated with 80% drop in adiposity and 2°C increase in temperature above brown and beige adipose tissue. Glucose intolerance was reversed, observed in both pair-fed and Nachbach groups. Food intake was reduced, but only contributed to 50% of the body weight effect, using a pair-fed control. Despite drop in adipose tissue and body weight, lean mass was preserved. Together, our data point to the potential of VMN^{PACAP} in reversing deleterious effects of high fat diet, particularly via effects in the brown and beige adipose tissue.

P132

Large Reductions In Bmi As An Analogue For Weightlessness In Space To Examine Brain Volumetric Changes

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Rationale: Long-duration astronauts show structural brain changes, including cerebral ventricular enlargement on post-flight brain imaging, following exposure to weightlessness. Large weight loss on earth also reduces tissue weight, offering a potential analogue for studying spaceflight-related brain changes. **Hypothesis:**

Large-magnitude weight loss results in brain volumetric changes resembling those during weightlessness in space. **Subjects:** Participants were grouped by bariatric surgery (BMI reduction ≥ 8 , $n=16$) and non-surgical Controls (BMI reduction ≤ 3 , $n=14$). **Procedures:** Data from magnetic resonance imaging (MRI) before and 4 months after surgery were analyzed. Total intracranial (TIV), cortical (CNV), ventricular (TVV), and white matter (WMV) volumes were calculated using FreeSurfer 7.4.1. Linear mixed-effects models assessed the interaction between BMI change and time. **Results:** TVV increased significantly in the weight loss (+2.2%) compared with the control group (-1.1% ; $p=0.017$). TIV decreased by 2.5% in the weight-loss group compared to 0.4% in controls ($p=0.016$). No significant differences were found for CNV or WMV. **Conclusions:** Substantial weight loss was associated with ventricular expansion and reductions in total intracranial volume. This could in part reflect changes in brain fluid content, such as seen with dehydration, where reduced blood volume and brain fluid volume are associated with increased ventricular and reduced total brain volumes. Both weightlessness exposure and weight loss reduce blood volume and venous pressure, which may partly underlie the similar changes. Weight-loss may provide an accessible analogue for investigating brain volume changes in microgravity.

P134

Ultra-Processed Foods Elicit Distinct Metabolic And Neural Responses Despite Nutritional Matching

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Food value is learned in part through post-ingestive metabolic signals that communicate nutritional content via the gut-brain axis. It is unknown whether the altered physical structure of ultraprocessed foods (UPF) modifies these signals and alters food reward, independently of caloric load and macronutrient composition. To test this, we recruited healthy weight adults ($n=57$) aged 18-45 years. First, to determine if food processing level alters postprandial metabolic response, nutritionally matched NonUPF and UPF meals (300 kcal) were consumed on separate days during 4-hour whole-room indirect calorimetry sessions with simultaneous blood draws. The UPF condition elicited larger insulinemic and energetic responses with attenuated carbohydrate oxidation (all $p<0.05$). Next, we examined the association between differing post-oral signals and food cue reactivity as measured by functional magnetic resonance imaging (fMRI). Processing-related differences in peak carbohydrate oxidation were associated with NonUPF versus UPF cue reactivity in the superior temporal gyrus, caudate, and ventral striatum (all $T>5$, $pFWE<0.05$). Finally, a Becker–DeGroot–Marschak auction task concomitant with fMRI was employed to evaluate whether value-related neural responses differed for NonUPF versus UPF. Although willingness-to-pay did not differ between conditions, value-related BOLD responses were greater for NonUPF than UPF in the fusiform gyrus, putamen, and caudate (all $T>4$, $pFWE<0.05$). These findings demonstrate that even when matched for nutritional profile, NonUPF and UPF produce different post-oral signals, and those signals influence brain response to food cues.

P136

Sustained Self-Generated States Of Enhanced Motivation Under Circadian Control

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Despite advances in understanding acute anticipatory reward-seeking mediated by discrete cues, mechanisms driving internally generated reward-seeking are unknown. Food anticipatory activity (FAA) is a robust cue-independent surge in locomotion that emerges hours before a predictable meal. However, it is unknown whether FAA also represents a self-generated state of enhanced motivation, which we call food anticipatory motivation (FAM). We developed an operant home cage task using Feeding Experimentation Devices v.3 where mice learn to nose poke for chocolate rewards during a designated one-hour period of the day [Zeitgeber Time (ZT) 18-19]. Motivation is measured during 1hr progressive ratio sessions at the following times: during the FAA window [ZT 17-18], active [ZT 5-6] or inactive phase [ZT 14-15]. During the FAA window, fasted mice that can predict feeding time increase both wheel running >40-fold and heightened effort-based motivation. However, mice that cannot predict mealtimes by random feeding timing acutely increase locomotor activity in response to hunger but fail to organize the heightened motivational state. Mapping of whole brain cFos, an indirect marker of activated neurons, revealed reorganization of cortical, striatal, and thalamic circuits implicated in reward-seeking behavior. Furthermore, preliminary studies with genetic ablation of dopamine receptors in these circuits suggest that dopamine signalling shapes FAA and FAM. Together, these findings describe how circadian processes underlie autonomous states of sustained enhanced motivation, bearing implication for disorders characterised by dysfunctional motivation, interoception, and circadian function, such as bipolar, depression, and substance use disorders.

P138

A Cortical-Serotonin Circuit For Feeding Regulation

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Rationale: Dysregulated food intake is a major driver of obesity, highlighting the need to define neural circuits governing feeding. While serotonergic therapies suppress appetite, adverse effects limit their clinical use. Understanding upstream cortical control of serotonergic feeding circuits may enable safer interventions. The agranular insular cortex (AIC), a hub for interoception and food processing, directly innervates dorsal raphe nucleus (DRN) serotonin (5-HT) neurons, but the functional role of this pathway remains unclear. **Hypothesis:** The AIC→DRN circuit bidirectionally regulates feeding and food processing through mixed excitatory and inhibitory synaptic mechanisms. **Species:** Mouse **Subjects:** 70-90 **Procedures:** Retrograde tracing, chemogenetic activation, chronic inhibition,

fiber photometry, electrophysiology, and feeding assays. Data were analyzed using t-tests or ANOVA with post hoc correction. **Results:** Retrograde tracing confirmed AIC projections to DRN neurons. Acute chemogenetic activation increased food intake in fed and fasted mice, whereas chronic inhibition reduced cumulative intake and attenuated post-fast refeeding. Fiber photometry revealed dynamic modulation of DRN-projecting AIC neuron activity during feeding.

Electrophysiology studies suggest co-release of GABA and glutamate from AIC to 5-HT^{DRN} neurons. **Conclusion:** These findings identify the AIC to DRN pathway as a regulator serotonin and feeding across homeostatic and cue-driven contexts and reveal a potential dual-transmitter mechanism of cortical control over serotonergic circuits, providing a promising translational target for maladaptive feeding and obesity.

P140

Identification Of Neurovascular Abnormalities In An Obesity-Cognitive Impairment Mouse Model

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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 mice develop cognitive impairment associated with **cerebral neurovascular abnormalities** using the inflow-based vascular space occupancy (iVASO) MRI approach developed by us. Transgenic SP1 mice at 3, 10, and 20 months of age were used as experimental subjects. We measured behavioral changes of these mice using the Open Field Test, Y-Maze, and Novel Object Recognition Test. We found that there were significant cognitive impairments 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 worse cognitive impairments. In contrast, at 3 months of age (starting point for obesity phenotype), there was no change in locomotor activity or cognitive function compared with non-transgenic mice. Using iVASO-MRI to measure cerebral blood volume in small pial arteries and arterioles (CBVa), we found that CBVa was decreased in both hypothalamus and hippocampus in obese SP1 mice compared with age-matched control mice. We further validate these brain changes by brain immunohistochemistry approaches using a blood vessel marker antibody. These results indicate that obese SP-1 mice displayed cerebral neurovascular abnormalities that may contribute to the development of obesity-linked cognitive impairments. These MRI measures may constitute non-invasive biomarkers for obesity-related cognitive impairment.

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Dorsal Vagal Complex Relaxin-3 Signaling- A Novel Target For Glycemic Regulation In An Obesity Model.

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Relaxin-3 is an orexigenic neuropeptide that is upregulated in obesity. As enhanced relaxin-3 signaling may drive hyperphagia and weight gain in obesity, antagonizing relaxin-3 signaling represents an attractive target to mitigate dysregulated feeding. The relaxin-3 receptor, RXFP3, has widespread central expression including in the Dorsal Vagal Complex (DVC) of the hindbrain. Most work surrounding relaxin-3 has focused on other energy balance areas like the hypothalamus, while no work to date has examined relaxin-3 action in the DVC. We set out to investigate the potential therapeutic contribution of targeting hindbrain RXFP3 in obesity, hypothesizing that antagonizing RXFP3 in a metabolically dysregulated Diet Induced Obesity (DIO) rat model would decrease feeding and bodyweight. While 4th ventricle (4V) administration of a RXFP3 antagonist, R3(B1-22)R, suppressed appetite in lean rats (n=8), basal food intake was unchanged in DIO rats (n=7-10). There was, however, still an increase in basal food intake following 4V injection of the RXFP3 agonist, [G(B24)S]R3/I5, in female but not male DIO rats (n=7-10). We next assessed oral glucose tolerance, finding that RXFP3 agonism worsened while antagonism improved glucose clearance in DIO females, while having no effect on males (n=5-9). These data are consistent with the reported higher sensitivity of females to relaxin-3 signaling. Characterization of the DVC RXFP3 population by fluorescent in situ hybridization (n=3-4) revealed 35.7% expression on GABA and 20.3% on glutamate neurons with no sex differences. These findings suggest that while other central sites of RXFP3 signaling may more strongly regulate appetite, we describe hindbrain RXFP3 as having a novel action to regulate glycemia in metabolic disease.

P144

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 behavioral deficits. While adverse consequences of food insecurity have been shown in humans, rodent models allow for greater control to assess long term effects. The mesolimbic dopamine system plays a critical role in modulating reward learning and decision-making. Stimulation of the medial forebrain bundle (MFB) using intracranial self-stimulation (ICSS) provides consistent and accurate decision-making behavior. We modeled food insecurity in adolescent rats (n=15) with a pseudorandomized feeding schedule, where insecure rats received four meals, one randomly omitted, alternating between 75% and 125% of 90% ad lib intake, while secure rats received 4 meals at 90% daily intake of age matched rats. Body weights were measured from weaning day until the completion of study. Blood glucose was measured after a 16hr fast and at intervals of 0 to 120 mins post glucose solution intake. Measurements were done before and after an 8-day HFHS diet challenge. Preliminary data shows a 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 lever press on FR1 schedule to determine amplitudes. We then measured how

well rats discriminate between “small” and “large” rewards (1 vs 3 pulse of stimulation). Finally, rats were tested on a delay discounting task where the delay for the “large” reward was increased to assess impulsivity. The effect of food insecurity on impulsivity and learning in adulthood will be assessed.

P146

Mesolimbic Dopamine Signaling Mediates Increased Hedonic Feeding And Food Seeking In Lactating Mice

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Lactation represents a critical physiological period that imposes significant energetic demands on mothers and impacts both maternal and offspring health. To meet the demands of milk production for their offspring, lactating mammals drastically increase food intake. However, the underlying behavioral, molecular, and neural circuit mechanisms driving increased feeding behavior during lactation remain poorly understood.

In this study, we investigated changes in feeding behavior and motivation in lactating mice using automated home cage feeding devices (FED3). Our results show that lactation alters meal patterns and increases food-seeking behavior, along with an increased preference for palatable foods in lactating mice (n=12-14). Given the known role of dopaminergic pathways in regulating food-seeking and hedonic eating, we employed pharmacological, chemogenetic, and imaging techniques to explore changes in these pathways during lactation.

In vivo fiber photometry experiments demonstrated increased dopamine responses in the nucleus accumbens of lactating mice in response to food (n=6-8). This elevated dopamine signaling was ultimately required for promoting both food seeking and palatable food intake during lactation as chemogenetic inhibition of VTA dopamine neurons reduced food seeking and palatable food intake in lactating mice to non-lactating levels (n=8-12). Further, selective inhibition of dopamine receptors using bilateral cannula implanted into the nucleus accumbens produces similar results (n=6-8).

Together, these findings provide evidence that the mesolimbic dopamine circuit mediates elevated food seeking and palatable food intake during lactation, providing novel insights into the regulation of maternal energy balance and feeding behavior.

P148

Inhibition Of Angiotensin Type-2 Receptor-Expressing Neurons In The Nucleus Of The Solitary Tract Reduces Food Intake And Metabolic Activity.

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Angiotensin II, the primary effector of the renin-angiotensin system, regulates cardiovascular function and fluid homeostasis partly via the nucleus of the solitary tract (NTS), a brainstem region which integrates cardiovascular and gastrointestinal signals. The NTS contains angiotensin type-2 receptor (AT2R)-expressing neurons (NTS^{AT2R}) that influence cardiovascular (e.g., baroreflex) function; however, their role in ingestive behavior and metabolism is unclear. We broadly hypothesize that NTS^{AT2R} neurons integrate interoceptive signals to coordinate cardiovascular and metabolic regulation, and here specifically tested whether they regulate feeding behavior and energy balance using a chemogenetic approach. Adult male AT2R-Cre mice received Cre-dependent inhibitory DREADDs (hM4Di) or control virus in the NTS. After surgical recovery, metabolic parameters were continuously measured (SABLE system) in a counterbalanced within-subject design [saline vs. clozapine-N-oxide (CNO); 1 mg/kg] during a fasting/refeeding paradigm. Preliminary results show that CNO-mediated inhibition of NTS^{AT2R} neurons significantly reduces energy expenditure and food intake relative to controls. These findings identify NTS^{AT2R} neurons as regulators of energy balance and potential brainstem target for both cardiovascular and metabolic disorders.

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A Topography-Based Bmi Predictive Model

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Most neuroimaging studies evaluating body weight rely on cue-evoked or resting-state paradigms that may not reflect real-world cognition and how the brain works during everyday tasks. In contrast, naturalistic viewing (NV) functional magnetic resonance imaging (fMRI) examines brain activity during more real-world-like settings, such as watching a movie. We hypothesized that individual-specific brain topographic patterns derived from NV fMRI would predict body mass index (BMI) ($r \geq 0.20$) using a topography-based predictive framework (TOPF). We used data from the Human Connectome Project 7T dataset. 89 healthy adults (females = 54) reported their height and weight and watched four short movie clips during fMRI scanning. We excluded participants with neurological or psychiatric disorders, diabetes, missing data, genetic relatedness, and excessive head motion (>25% of frames with FD ≥ 0.5 mm). We used Glasser and FreeSurfer atlases to parcellate preprocessed brain data into 379 cortical and subcortical regions. Principal component analysis extracted individual-specific expressions of shared neural responses, which were used as features in ridge regression model to predict BMI. We evaluated model performance using 10-fold cross-validation with Pearson correlation (r) and coefficient of determination (R²). We regressed out the effects of age, sex, and head motion before evaluating prediction performance. Preliminary results showed weak prediction accuracy (Pearson $r = 0.13$) with near-zero explained variance (R² = -0.001), indicating minimal generalizable predictive performance. Brain activity during a general NV task does not appear to predict BMI. NV tasks that involve food or eating may elicit a stronger relationship between BMI and brain activity.

P152

Does Loss Of Neurotensin Expression Within The Lateral Hypothalamic Area Of The Brain Promote Comorbid Obesity And Pain?

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There is a gap in treatment for comorbid obesity and chronic pain, as weight loss medications do not treat pain and many analgesics cause weight gain. Neurotensin (Nts) is a peptide with potential to simultaneously support weight loss and analgesia. Indeed, activating Nts-expressing neurons in the lateral hypothalamic area (LHA) of the brain increases locomotor activity and reduces feeding, body weight and pain. However, LHA^{Nts} neurons release Nts as well as GABA, corticotrophin releasing hormone (CRH), and galanin, posing the question: which signal mediates the beneficial weight and analgesic effects? We hypothesize that Nts is the critical signal, such that depleting Nts from the LHA will promote weight gain and pain. To test this, we injected Nts^{flox/flox} mice in the LHA with either AAV-GFP (Controls with intact LHA^{Nts} neurons) or AAV-Cre-GFP to selectively deplete Nts expression (Nts Depleted). Nts Depleted mice have increased body weight on chow and high-fat diet and have increased pain sensitivity compared to Controls. Moreover, Nts Depleted mice have increased operant responding for sucrose but reduced amphetamine-induced locomotor activity; these behaviors suggest impairment of the mesolimbic dopamine system that is critical for modulating motivated feeding and movement. Taken together, these data suggest that Nts expression within the LHA is important for restraining development of obesity and comorbid pain, at least in part via the mesolimbic system. Going forward, these findings could inform future design of approaches to restore or augment Nts signaling to support healthy weight and pain relief. This work was supported by awards from the United States Department of Defense (HT9425-23-1-0579) and the NIH (3-R01-DK103808).

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Low Protein-Induced Fgf21 Reprograms Developmental, Structural, And Molecular Trafficking Hypothalamic Gene Networks During Aging

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Dietary protein restriction (DPR) is a dietary intervention that extends healthspan in a fibroblast growth factor 21 (FGF21)-dependent manner. FGF21, a liver-derived hormone, acts on the hypothalamus to inhibit mTOR and increase thermogenesis, insulin sensitivity, and fatty acid oxidation. Collectively, these mechanisms improve metabolic health during aging. Although recent studies demonstrated that feeding-related pathways in the hypothalamus are upregulated in young mice, the effects of DPR-induced FGF21 at old age is unclear. We investigated DPR-induced hypothalamic remodeling and corresponding metabolic outcomes in late-middle-aged males. At 15 months of age, 10 male mice were fed a normal-protein or low protein (LP) diet for 26 weeks. Metabolic health was evaluated with fasting glucose levels, glucose tolerance tests, and body composition. At 22 months of age, the hypothalamus was microdissected for bulk RNA sequencing. Gene set enrichment analyses demonstrate that LP-induced FGF21 regulates structural and synaptic processes, while over-representation analyses (ORA) identify regulation of ion transport. Consistent with previous studies, mTOR was downregulated in LP-fed animals. These molecular changes correspond to improvements in metabolic health, including increased thermogenesis, glucose clearance, and reductions in body weight and fat mass. Our results indicate DPR initiation at late middle age in males improves metabolic health. Further, transcriptional signatures of cellular structural remodeling show that DPR not only initiates feeding-related pathways in the hypothalamus but also alters neuronal plasticity and neurogenic processes. Finally, DPR-induced regulates membrane potential and synaptic by enriching for hypothalamic ion transport genes, as identified by ORA.

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Eloralintide, An Amylin Type 1 Receptor Preferential Agonist, Suppresses Food Intake And Reduces Body Weight Without Inducing Illness Behaviors

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Amylin and calcitonin receptor (CTR) agonists are emerging as next-generation treatments for obesity and type 2 diabetes, but nausea/emesis associated with these therapies limit patient adherence. Amylin analogues act via amylin receptor (AMYR) complexes, formed by CTRs heterodimerizing with one of the receptor activity-modifying proteins (RAMP1/2/3). Eloralintide is an amylin type 1 receptor (AMY1R) preferential agonist under investigation for treating obesity with favorable GI tolerability. The mechanisms on how preferential AMYR agonists versus dual amylin and calcitonin receptor agonists (DACRA) regulate food intake, along with their nauseating side effects, have not been systematically evaluated. This study utilizes eloralintide to preferentially activate AMY1Rs and investigates the hypothesis that AMY1R preferential activation induces a different tolerability and behavioral profiles than DACRAs. In both lean and DIO male and female rats, eloralintide dose-dependently decreased food intake and suppressed body weight, without inducing nausea-like pica behavior, whereas multiple DACRA analogues tested elicited food intake suppression along with significant pica behavior in rats. Eloralintide had overall less neuronal activation in the DVC-LPBN-CeA circuit implicated in mediating nausea/emesis compared to DACRAs, aligning with the behavioral profiling. We also found that eloralintide suppressed meal number in the first 24h post administration, while the anorexia post 24h showed suppression in meal size. Lastly, eloralintide impacted motivational aspects of feeding in operant condition paradigms. Together, these data show how AMY1R selective agonism modulates feeding without inducing malaise, suggesting AMY1R agonism as a potential obesity therapy. (NIDDK-105155)

EffectS Of Non-Nutritive SWEETENER Consumption ON Blood Metabolic Response

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Non-nutritive sweeteners (NNS) have grown popular as a sugar substitute, as they mimic the sweetness of nutritive sweeteners (NS) but provide no calories. More recently, the beverage market has expanded to include combinations of NNS and NS but little is known about their metabolic effects. In this study, participants (n = 39) received either a NS, NNS, or combination (NS+NNS) drink, with blood samples collected before and after consumption. Within that group, participants (n = 21) had multiple unannounced 24-hour dietary recalls. The aim of this study is to investigate the effect of NNS on metabolic blood measurements, and whether habitual NNS consumption influences the results. We examined the effect of condition on blood glucose area under the curve (AUC) and the relationship of AUC across levels of habitual NNS consumption (aspartame, saccharin, sucralose, acesulfame potassium) and added sugar, depending on drink condition. We observed a difference in blood glucose AUC evoked by the NNS drink vs others ($p < 0.001$), and a small difference between the NS and NS+NNS condition ($p_{\text{corrected}} = 0.097$). Higher habitual consumption of aspartame, however, interacted with this effect, specifically it was associated with lower glucose AUC after consuming the NS+NNS ($p = 0.003$), but not the others. There was also a positive correlation between baseline glucose levels and aspartame consumption ($p = 0.006$). Sucralose (via mass spectrometry) and insulin (ELISA) are still under analysis. Investigating the effect of NNS+NS combinations on metabolism and how they interact with NNS consumption is essential to understanding the metabolic effects of products already in the market and provide insight for better health choices to combat obesity and related diseases.

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The Effect Of Adding Seaweed To A Meal On Mastication Rate In Young Healthy Males

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Rationale: Food texture described as “chewy” contributes to the regulation of satiation, satiety and food intake by affecting pre- and post-ingestive satiety signals. One strategy to enhance satiety signalling is to develop food products with added ingredients that increase mastication without compromising palatability. Hypothesis: Adding seaweeds to traditional meals will increase the mastication rate. The objective was to investigate the effect of adding seaweeds to a breakfast meal on mastication rate in young healthy adults. Methods: In a single-blinded crossover, ten young healthy males (24.1 ± 4.5 y) attended two sessions and were asked to consume an omelette containing 5g of *Chondrus crispus* seaweed or the same omelette without added seaweeds in a counter-balanced order. Procedure: The participants were served with a freshly prepared meal and asked to consume it at their regular pace. The eating behaviour was analyzed from video-recorded food consumption and subsequent bite analysis, using the Consumption Behaviour Module in Face Reader 9 (Noldus, Wageningen, the Netherlands). Data analysis: the data were tested for normality using the D'Agostino & Pearson test, and the difference between treatments was analyzed using a paired t-test or the Wilcoxon matched-pairs signed-rank test for non-normally distributed data. Results: Adding seaweed to a meal led to a 1.5-fold increase in chew cycles per bite ($P=0.002$) and a 1.5-fold reduction in bites per minute ($P=0.003$) compared to the meal without seaweed. The ingestion rate (grams per minute) was lower with a meal containing seaweed compared to the meal without seaweed ($P=0.04$). Conclusion: Adding seaweed to a meal increases mastication and may be used to control ingestive behaviour.

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Highly Selective Amy1R Agonist Antibodies For Next-Generation Obesity Treatment

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Agonists targeting the Amylin receptor (AMYR) are a key next-generation obesity therapeutic class, positioned to overcome significant gastrointestinal (GI) side effects limiting patient persistence with GLP-1R drugs and dual amylin-calcitonin receptor agonists. Non-specific agonism of the Calcitonin Receptor (CTR) and AMY3R is linked to nausea and vomiting, driving the hypothesis that highly selective AMY1R agonists will maximize efficacy (satiety) while minimizing GI adverse events. Generating such specific agonists is challenging due to the high structural homology among CTR and AMYR subtypes (AMY1R and AMY3R are composed of CTR in complex with RAMP1 and RAMP3, respectively). Abalone Bio leveraged its Functional Antibody Selection Technology (FAST), which measures sequence-activity relationships of millions of antibodies to uniquely power ML-driven agonist discovery, to identify and optimize a novel class of

AMY1R agonist antibodies. These antibodies were tested by measuring intracellular cAMP accumulation in CHO-K1 cell lines specifically expressing CTR or AMYR receptors. Multiple antibodies demonstrated potent activity on AMY1R cells (comparable to pramlintide and salmon calcitonin) but showed low potency on human CTR and AMY3R cells. These antibodies possess a best-in-class specificity profile, exhibiting >200-fold AMY1R selectivity over CTR and cross-react with rat AMY1R, enabling in vivo studies in rat obesity. This selectivity is substantially greater than existing AMYR-specific peptides (e.g., pramlintide, eloralintide). These highly selective AMY1R agonist antibodies represent a novel therapeutic modality with the potential for long-acting, reduced side-effect treatment of obesity.

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Iba1⁺ Cells In The Nodose Ganglion Mediate Gut-Brain Axis Disruption In High-Fat Fed Rats

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Obesity is a growing global health concern that increases risk for chronic diseases such as heart disease and diabetes. The vagus nerve relays post-ingestive signals from the gut to the brain via afferents terminating in the nucleus tractus solitarius (NTS). Chronic high-fat (HF) feeding reduces vagal sensitivity to distension, nutrients, and satiety peptides and decreases postprandial NTS activation, promoting increased meal size and weight gain. We previously showed that HF feeding drives withdrawal of vagal afferent inputs to the NTS, evidenced by reduced isolectin B4 labeling of C-fibers. Vagal afferent cell bodies reside in the nodose ganglion (NG), and pharmacological depletion of NG Iba1⁺ immune cells prevents HF-induced vagal fiber loss. Here, we tested whether activation of NG Iba1⁺ cells promotes obesogenic phenotypes independent of diet. Using RNAScope in NG from male Wistar rats fed HF or chow for 4 weeks, we observed increased expression of microglial markers (TMEM119, P2RY12) and the macrophage marker EMILIN2 in Iba1⁺ cells of HF animals, indicating recruitment or expansion of myeloid populations. To test causality, we bilaterally injected AAV encoding a CD68-driven DREADD or GFP into the NG. Acute activation with clozapine-N-oxide (CNO) increased 4-hour food intake in DREADD-expressing rats versus controls. In vitro, 40–55% of Iba1⁺ cells co-expressed mCherry after CNO exposure, confirming targeting. Chronic activation via intraperitoneal osmotic CNO delivery increased food intake and body weight within 2 weeks. These findings identify NG Iba1⁺ cell activation as a driver of obesity and implicate immune-mediated disruption of vagal gut–brain signaling during HF feeding.

Friday, August 7, 2026

9:00 - 10:00 AM

Regency C & Foyer

Poster Session 3, Exhibits & Coffee Break

P202

Do Problematic Mealtime Behaviors Mediate The Association Of The Obesogenic Home Food Environment With Diet Quality?

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Rationale: Unhealthy foods in the home are associated with lower child diet quality. However, whether these foods prompt greater problematic child mealtime behaviors (e.g., food refusal, tantrums) is unknown. Hypothesis: Greater snacks and sweets in the home are associated with more problematic mealtime behaviors and subsequent diet quality through early childhood. Number of subjects: 187 children assessed at ages 3.5, 5, 6, and 7 years. Procedures: Measures included the snacks, sweets, sugared cereal, and sugar-sweetened beverage availability and accessibility subscales of the Home Food Inventory (HFI-SS), the Meals in Our Household Questionnaire problematic mealtime behaviors subscale, and the Healthy Eating Index (HEI) total, adequacy, and moderation scores calculated from 24-hour dietary recalls. Paired t-tests and correlations examined bivariate associations. Cross-lagged panel models tested associations of HFI-SS with mealtime behavior from ages 3.5-7 years. Results: HFI-SS availability increased (mean diff: 0.77, $p=0.04$) and accessibility decreased (mean diff: 0.23, $p=0.04$) from ages 3.5 to 5 years but were stable from ages 5-7 years. Problematic mealtime behaviors remained constant over time. HFI-SS accessibility was negatively correlated with HEI and HEI adequacy at age 3.5 ($r=-0.18$, -0.20 ; $p=0.04$, 0.02) and 5 ($r=-0.20$, -0.24 , $p=0.02$, 0.008), but only with HEI adequacy at age 6 ($r=-0.22$, $p=0.04$). HFI-SS availability was negatively correlated with HEI and HEI adequacy at age 5 ($r=-0.20$, -0.23 ; $p=0.03$, 0.009) but not at ages 3, 6, or 7. HFI-SS was not associated with problematic mealtime behaviors cross-sectionally or longitudinally. Conclusions: Associations of HFI-SS with diet quality were not attributable to problematic mealtime behaviors.

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Characterization Of Eating Behaviors In Response To Visual Food Cues In Adolescents With Restrictive Eating Disorders

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Severity of illness for restrictive eating disorders is often determined by weight loss and body mass index (BMI). Previously we demonstrated that anxiety-to-eat is a core feature in adults with anorexia nervosa (AN). Yet, little is known regarding eating-related anxiety in adolescents with restrictive eating disorders in general. Here, 49 adolescents (12-26 years old) receiving outpatient care and who met the DSM-5 criteria for AN (Restricting Type, $n=32$; Binge/Purge Type, $n=7$; or Atypical AN, $n=5$) or Avoidant/Restrictive Food Intake Disorder (ARFID, $n=5$) completed a food task in which they indicated their frequency of consumption and rated their level of liking, fullness, and anxiety-to-eat in response to images of 20 different foods varying in energy density. Adolescents with atypical AN had a higher BMI than all other groups and had lost significantly more body weight in the past six months relative to adolescents with ARFID and AN restricting. In response to visual food cues, adolescents with atypical AN had higher anxiety relative to those with the restricting subtype and higher perceived fullness relative to those with AN restricting or ARFID. Adolescents with AN restricting showed higher food liking relative to adolescents with ARFID. No differences in frequency of consumption of foods were observed across groups. These data demonstrate that despite a higher BMI, treatment seeking adolescents with atypical AN showed features associated with more severe pathology relative to groups with characteristically lower BMI, indicating the importance of considering eating-related behaviors and attitudes beyond BMI when determining severity of illness.

P204

Acute Semaglutide Administration Disrupts Performance In A Sweet Caloric/Non-Caloric Discrimination Test And A Water-Glucose Categorization Psychophysical Task Via Its Anorexigenic Effects

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Semaglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist, is well established for treating obesity; nevertheless, its role in modulating caloric and gustatory processing remains unexplored. To examine the acute and time-course effects of semaglutide on taste perception, C57BL/6 mice were continuously monitored in their home cage using a custom-built "Homegustometer." Two groups were trained on complementary tasks: a caloric/non-caloric preference test — in which two

fixed sippers delivered glucose (18%) or saccharin (0.1%), with solution identity pseudorandomly reassigned across lick-count blocks (25, 50, 100, 200, and 400 licks) — and a water–glucose categorization task assessing psychophysical discrimination. A single semaglutide dose induced ~12% body weight loss, recovering within 96 hours, paralleling behavioral effects in both tasks. Semaglutide reduced total intake regardless of solution identity and selectively attenuated glucose preference in the shortest blocks (25 licks), suggesting impaired rapid caloric discrimination. In the categorization task, accuracy dropped transiently from 75% to ~60% for ~24 hours, driven by miscategorization of water as sweet, with full recovery thereafter. The absence of conditioned taste aversion and full recovery of ingestive motivation in both tasks suggest specific modulation of gustatory processing rather than malaise. Beyond its hypophagic effects, semaglutide disrupts rapid caloric discrimination and gustatory categorization, revealing a novel role in chemosensory processing.

P205 **Thirty Years Later: Reexamining Rozin’s Desert Island Nutrition Question In A Contemporary U.S. Sample**

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In 1996, Paul Rozin published influential findings describing dichotomous thinking about foods (DTAF), the tendency to categorize foods as “good” or “bad.” Study subjects imagined being stranded on a desert island with fresh water and oranges growing on trees. They were asked to select one additional food that would be “best for health” from corn, alfalfa sprouts, hot dogs, spinach, peaches, bananas, and milk chocolate. Despite the importance of energy sufficiency for survival under extreme scarcity, few participants selected hot dogs or milk chocolate, the two energy-dense foods most capable of sustaining life. To examine to what degree DTAF persists, an online survey was conducted in February 2026 among 1,039 U.S. adults through a third-party market research firm. Respondents completed the original desert island nutrition question as part of a 10-item survey assessing perceptions of healthy eating. Bananas (32.8%) and spinach (29.4%) were most frequently selected. Only 13.9% selected either hot dogs or milk chocolate. Significant sex [χ^2 (1, N=1,039) = 8.23, $p=0.004$] and generational [χ^2 (3, N=1,030) = 8.09, $p=0.044$] differences emerged, with males and younger generations being more likely to choose energy-dense options vs. females and older generations. No significant differences emerged by household income, education level, BMI, or personal definitions of a healthy diet. Findings closely replicated Rozin’s original observations, suggesting DTAF remains common among contemporary U.S. adults. Although typical food environments are characterized by variety and abundance, DTAF may still undermine healthy eating by promoting rigid, oversimplified food judgments that contribute to nutritionally imbalanced or unsustainable dietary patterns.

P206 **Does Energy Density Affect Flavor Recognition Memory?**

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In animal models, learned flavor-nutrient associations produce strong flavor preferences and increased intake, but such effects have often been difficult to obtain in controlled human experiments. That may be partly due to choice of outcome measurements (i.e., should learning produce changes in liking, wanting, intake, satiation, etc.) and also participants’ extensive prior history with flavors. Here we tested whether energy density influences *flavor recognition memory*. After a single experience with a novel flavor, will people form a more accurate memory representation if the flavor was accompanied by higher energy density? We tested two distinctly different populations: United States university undergraduates, and Samburu Kenyans (who eat a simpler, considerably less varied diet with minimal exposure to ultra-processed foods). In each experiment, participants sampled four novel flavors, all rated as relatively unfamiliar and neither strongly liked or disliked. Then each participant consumed 400 ml of one of those flavors, randomly assigned to either low (32 kcal) or high energy (192 kcal maltodextrin). The next day participants sampled all four flavors again and attempted to identify which one they consumed the previous day. In both populations recognition memory was better than chance but relatively poor. Surprisingly, energy density during initial consumption did not improve recognition accuracy, and in fact among Samburu people recognition was slightly but significantly poorer in the high energy condition. These results will be discussed in the context of mechanisms of memory encoding and flavor evaluation.

P207 **Considering Flavor-Flavor Learning In Flavor-Nutrient Learning Paradigms**

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Flavor-nutrient learning (FNL), in which a flavor stimulus is paired with the post-ingestive consequences of calorie consumption is hypothesized to guide eating behavior and influence flavor preference. However, flavor-flavor learning (FFL), the pairing between a flavor cue and another flavor, may confound interpretations derived from FNL paradigms. As such, this study assessed FFL with sweetness. Human participants (N = 8; BMI = 27.1 kg/m²) tasted and rated 10 theoretically sweet-matched, non-caloric flavored solutions on perceptual qualities, including sweetness intensity, liking, and wanting. Flavors that were rated similarly low in liking and familiarity were randomized to a 0-kcal sucralose (CS-), 110-kcal sucralose + maltodextrin (CS + M), or 110-kcal sucrose (CS + S) drink condition. Using a randomized, crossover design, participants consumed each drink 6 times over 1 week (conditioning period), then tasted and rated each drink condition pre- and post- conditioning. We observed no differences in pre- to post- test change in sweetness (χ^2 (2, N = 8) = 0.37, $p = 0.83$), wanting (χ^2 (2, N = 8) = 0.94, $p =$

0.62), or liking ($\chi^2(2, N = 8) = 3.17, p = 0.20$) ratings across conditioning groups. To examine if individual differences in sweet perception influenced FFL, we assessed the effects of change in sweetness on pre- to post- test change in liking and wanting. We observed a main effect of change in sweetness ratings on change in liking ($\chi^2(1, N = 8) = 4.26, p = 0.04$) and wanting ($\chi^2(1, N = 8) = 5.95, p = 0.01$) ratings where increased change in sweetness ratings was associated with increased change in liking and wanting ratings. These data emphasize the need to account for potential effects of FFL on designs and analyses of FNL paradigms.

P208

Post-Covid Condition, Not Chemosensory Impairment, Predicts Weight Change Through Dietary Behavior Mediators.

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Rationale/Premise: COVID-19 causes smell and taste impairment in some patients, potentially affecting appetite and body weight. Food noise is persistent, unwanted food-related thoughts. We hypothesized an association between chemosensory impairment (CI), Post-COVID Condition (PCC), food noise, and post-COVID weight change, and considered whether dietary behaviors mediate these relationships. Methods: Adults (N=855) with COVID-19 were surveyed and classified as chemosensory never impaired, impaired but recovered, or currently impaired. PCC score (4-item scale, lower means greater severity), food noise (RAID-FN Inventory), and percent weight loss were assessed. Adjusted regression and mediation analyses examined food noise, dietary restraint, loss of control eating, and dieting frequency as mediators of the relationship between PCC and weight change. Results: CI predicted higher food noise ($\beta = 0.093, p < 0.001$) but not weight loss ($p = .262$). PCC severity predicted higher food noise ($\beta = -0.326, p < .001$), loss of control eating ($\beta = -2.517, p < .001$), less dietary restraint ($\beta = 0.253, p = .010$), and less weight loss ($\beta = .012, p = .020$). Food noise did not mediate PCC-weight change (mediated $p = .158$). Loss of control eating mediated this relationship (mediated $p < .001$); dietary restraint partially mediated it (mediated $p = .012$). Conclusions: PCC, not CI, is associated with food noise elevation and changes in post-COVID weight loss. PCC effects on weight may operate through loss of control eating and dietary restraint, not food noise. Interventions targeting loss of control eating may be particularly important for managing weight-related consequences of PCC, and food noise appears unlikely to represent a behavioral mechanism linking PCC to weight loss.

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Validation Of A Context-Specific Fullness Questionnaire As A Predictor Of Eating-To-Capacity And Portion-Based Fullness Judgments

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To test the ecological validity of fullness ratings made after meals eaten to capacity in a laboratory, and portion sizes displayed on a computer screen, we used a validated, 2-scale, context-specific questionnaire (CQ) that assesses fullness in recalled eating situations (SSIB 2026). Candidates for metabolic and bariatric surgery (MBS) and normal-weight controls (NWC) completed three tasks: (1) rating recalled fullness after the “largest meal ever eaten” using the CQ, (2) rating expected fullness in response to a 969 kcal virtual portion of Ensure® (POR), and (3) rating fullness after consuming an Ensure® meal to capacity in the laboratory (CAP). CQ ratings were compared with fullness ratings obtained during CAP (N = 73 MBS and 33 NWC) and POR (N = 57 MBS and 24 NWC). Ratings were categorized into four quadrants using upper-third cut-offs on both visual analog scales (VAS) and general VAS (GVAS) to improve precision. For comparisons of CQ and CAP ratings, with groups and scales combined, significantly more observations fell in high-high and low-low concordant (N = 81) than discordant (N = 35) quadrants (McNemar $\chi^2 = 6.43, p < 0.01$). There were no significant differences by group or scale ($\chi^2 = 1.15, p = 0.29$). For comparisons between CQ and POR, significantly more concordant (N = 63) than discordant (N = 8) observations were observed for VAS ($z = -6.52, p < 0.001$), but not for GVAS (N = 34 for concordant vs. N = 38 for discordant $z = -0.47, p = 0.64$), with groups combined. These findings not only indicate that the CQ, when used with VAS, is a useful tool for assessing concordance with instructions to eat to capacity and to rate fullness in response to displayed portions, but also that participants consistently rate fullness based on visual stimuli and recalled experiences in relation to actual eating. Support: NIDDK_R01DK108643.

P210

Validity Of Recalled Appetite-Related Ratings Across Eating-Related Contexts

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Appetite ratings have been used to measure hunger and satiation during laboratory eating. Can people actually quantify these feelings and relate them to real life?

We, therefore, measured the discriminant validity of appetite ratings by significant differences in remembered feelings across eating-related contexts, during screening and training before laboratory eating. 91 candidates for bariatric surgery, and 51 normal-weight individuals, rated remembered feelings of “hunger”, “fullness”, “sickness”, and “thirst” across eating contexts of: “normal dinner”, “small snack”, “largest meal” and “something that disagreed”. Ratings were made on both 150 mm general visual analog scales (GVAS) and VAS, with top anchors: “strongest experienced sensation of any kind” and “extremely”, respectively, and were subjected to mixed model ANOVA with group, scale, context, and feeling as independent variables. Conservatively, we report only the smallest significant differences for GVAS for normal-weight participants, because there were interactions of group x context x question. As expected, there were significant (SED’s = 9.0, $p < .05$) differences across contexts for mean (mm) $\pm$ SE (± 6.66) “fullness”: snack (59), dinner (81), and largest meal (99). “Fullness” for disagreed (65) was not significantly different from snack or dinner. In contrast “sickness” for disagreed (91) was greater than for large meal (48) or snack (19). All these differences were larger for VAS ratings and for GVAS and VAS ratings made for the bariatric surgery group. We conclude that people can quantify appetite-related sensations which could be used to determine what real-life contexts are being rated in the laboratory and in ratings of visualized portions shown on a computer screen. (support: NIDDK_R01DK108643)

P211 **Psychosocial Correlates Of Dietary Intake And Cooking Behavior Among Adults: Results From A Pilot Community Cooking Intervention**

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Dietary behaviors and psychosocial factors, including well-being and perceived stress, may influence food choice and overall diet quality. Interventions incorporating cooking and nutrition education may improve these domains; however, their interrelationships are not well characterized. We hypothesized that participation in a 6-week cooking intervention single-arm pilot would improve food-related skills, dietary intake, and psychosocial outcomes over time, and that changes in psychosocial factors would be associated with changes in diet quality. Adult participants (n = 19) completed assessments at baseline (T1), post-intervention (T2), and follow-up (T3). Outcomes included perceived stress (PSS), food agency (self-efficacy), PERMA well-being domains, and diet quality assessed by the Healthy Eating Index (HEI). Linear mixed-effects models with random intercepts for participants were used to examine changes over time and within-person associations. Food agency increased significantly over time ($F(2,68) = 50.03$, $p < .001$), with sustained improvements at T2 and T3. No significant changes were observed for HEI or PSS ($p > 0.05$) over time. In within-person models, changes in well-being (PERMA) were positively associated with HEI ($\beta = 1.15$, $p = 0.41$), while changes in perceived stress were not associated with HEI ($\beta = 0.21$, $p = 0.55$), neither was statistically significant. In this pilot study, results suggest a within person improvement in self-efficacy and well-being measured by PERMA. These findings support a potential pathway by which cooking behavior interventions may influence psychosocial health and possibly food choice. Larger, adequately powered studies are needed to evaluate broader psychosocial and dietary effects.

P212 **The Nausea Atlas: Identifying And Characterizing Nausea Subtypes Using Patient-Reported Information**

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Across the practice of medicine, nausea is a common and poorly understood symptom. Although many interventions are available to treat nausea, there is little evidence to guide the prioritization of treatment options. We hypothesized that comprehensively cataloging and organizing the experiences of patients with nausea can elucidate associations between certain clinical factors and particular treatments’ effectiveness. We performed an online survey of patients recently diagnosed with nausea, who answered over 200 multiple-choice questions. We collected 3,669 complete descriptions of nausea experiences. There was a high overall burden of nausea, in terms of chronicity, severity, and debilitation. Among all respondents, ondansetron was the most effective treatment, followed by promethazine, lorazepam, and marijuana. Benzodiazepines were particularly helpful for those who experienced anxiety in association with nausea. Principal components analysis of the descriptors of nausea revealed several physiologic domains that delineated the range of respondents’ experiences; these included sensitivity to smells and tastes, cephalic (CNS/vestibular) involvement, abdominal discomfort, emotional distress, gastro-esophageal reflux, vomiting, and dysautonomia. Among the major causes of nausea, GLP-1 agonist medications were found to have the lowest applicability rating for nearly every nausea descriptor, suggesting a detachment from most nausea-associated processes in the periphery. To our knowledge, this is the first large-scale and comprehensive characterization of patients with chronic, severe nausea. It provides a novel evidence basis for nausea treatment guided by clinical characteristics, and it highlights the potential to uncover basic knowledge about nausea mechanisms.

P213 **Modeling Reward-Based Overeating: Characterizing Neural Circuitry Contributing To An “Overconsumption Prone” Phenotype**

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Obesity is a growing public health epidemic in the United States, affecting over 40% of adults and nearly 20% of children, with the few available treatments offering limited efficacy. Several brain regions engaged during feeding overlap with core components of the reward system, indicating that evaluating patterns of food intake and consummatory behaviors through the lens of reward processing may reveal important mechanisms underlying consumption and overconsumption. Reward-based overeating represents an under-examined disorder distinct from other eating disorders that may contribute to the pathophysiology and prevalence of obesity. It is characterized by persistent hedonic eating, overeating past the point of satiety, tolerance and withdrawal, and a

significant disruption to daily life. We have developed mouse models prone and resistant to reward-based overeating. These models enable the identification and characterization of behaviors and neurochemistry associated with reward-based overeating to elucidate differences in the underlying neural circuitry. We hypothesize that specific aspects of the dopamine circuitry in the dorsal striatum predisposes some individuals to reward-based overeating. This study will utilize our “overconsumption prone” mouse model to characterize the neurochemistry underlying this behavior, prior to and following the onset of palatable food intake. Characterization of the neural circuitry underlying reward-based overeating will allow for identification of predisposing and modulating neural correlates of reward-based overeating, furthering development of potential interventions in treating and preventing obesity.

P214 **Sbi-553 Suppresses Food Intake And Weight Gain In Hungry Mice**

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Obesity affects >40% of the U.S. population, underscoring the need for safe, effective treatments. Neurotensin suppresses feeding and promotes weight loss in rodents via neurotensin receptor 1 (NtsR1), which signals through both β -arrestin and Gq pathways. However, NtsR1 activation also induces adverse side effects such as hypothermia and hypotension (thought to be mediated by Gq signaling), which has limited the clinical potential of this ligand-receptor system. SBI-553, a novel β -arrestin-biased allosteric modulator of NtsR1, has potential to avoid these adverse effects. Published work shows that SBI-553 reduces intake of pharmacological rewards (psychostimulants, ethanol) and pain without producing the negative side effects associated with Gq signaling. We therefore hypothesized that SBI-553 would suppress intake of natural rewards (food) and promote weight loss in mice. To test this, regular-weight and diet-induced obese mice were treated with either SBI-553 (12 mg/kg, i.p.) or saline in a crossover study design. Mice underwent metabolic profiling under homeostatic conditions with ad libitum access to food and water as well as fasting-induced refeeding. Paired t-tests showed that under homeostatic conditions, SBI-553 acutely suppressed feeding in male obese mice (n=7, p<0.05) without altering other metabolic measures. When mice were fasted to induce hunger, SBI-553 treatment suppressed refeeding and weight gain in regular-weight (n = 9 males, 7 females, p<0.05) and obese mice (n = 7 males, 8 females, p<0.01–0.05). Together, these results suggest that SBI-553 suppresses feeding and weight gain in the face of enhanced feeding drive. In the future, SBI-553 might be useful to restrain feeding during high appetitive drive states such as dieting to support weight loss.

P215 **Neuronal Hypothalamic Fibroblast Growth Factor-1 Signaling Is Required For Normal Energy And Glucose Homeostasis And For Protection Against Diet-Induced Obesity.**

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A single intracerebroventricular (icv) injection of fibroblast growth factor-1 (FGF1) induces both transient anorexia and weight loss and sustained remission of diabetic hyperglycemia in rodent models of type 2 diabetes (T2D) via actions involving the mediobasal hypothalamus (MBH) of the brain. While FGF1 is endogenously expressed in the MBH, its physiological role in regulation of energy homeostasis is unknown. We hypothesized that endogenous FGF1 signaling in the MBH is required for normal regulation of energy balance. To test our hypothesis, we selectively deleted FGF1 from the MBH neurons of adult male FGF1-floxed mice by microinjecting either control AAV1-CAG-GFP (n = 8) or AAV1-hSyn-Cre-WPRE.hGH (n = 7) into the MBH bilaterally. The mice were initially chow-fed then switched to high fat diet (HFD) while we conducted comprehensive physiological assessments in indirect calorimetry metabolic chambers. We report that FGF1 deletion specifically from MBH neurons resulted in increased bodyweight and body adiposity (*p<0.05, two-way ANOVA) in chow-fed mice. We also observed disruption of circadian patterns of feeding and locomotion, in which animals consumed a greater proportion of food intake during the light cycle followed by decreased dark cycle and daily locomotor activity (*p<0.05, two-way ANOVA). Interestingly, these phenomena were robustly exacerbated when the mice were switched to HFD. HFD consumption exaggerated obesogenic phenotype, characterized by hyperphagia, reduced energy expenditure and locomotion, and glucose intolerance (*p<0.05, two-way ANOVA) in FGF1-deleted mice. Based on these findings, we conclude that endogenous FGF1 signaling by MBH neurons is required both for normal energy and glucose homeostasis and protection against diet-induced obesity.

P216 **Insulin Regulation Of Alcohol Intake**

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Alcohol use disorder affects ~28.6 million U.S. adults. Glucagon-like peptide-1 receptor (GLP1R) agonists increase plasma insulin and reduce alcohol (EtOH) intake, implicating insulin mechanisms in EtOH consumption. Insulin is a satiety hormone disrupted by EtOH, but whether reducing insulin signaling drives escalated EtOH intake is unknown. We hypothesized binge EtOH reduces plasma insulin, leading to an increase in EtOH intake. Adult male and female C57BL/6J mice (N=40) underwent 3-day EtOH vapor or air exposure and tested 4h post-binge. Student's unpaired t-tests showed binge EtOH significantly increased plasma glucose, decreased plasma insulin, and increased pancreatic islet insulin immunoreactivity, suggesting binge EtOH increases insulin sequestration. In a separate

cohort, 8 female mice were trained to drink 15% EtOH in a two-bottle choice paradigm, underwent 3-day EtOH vapor exposure, and retested 4h post-binge. Paired t-tests revealed intranasal insulin administration reduced EtOH intake and preference vs intranasal saline, suggesting insulin regulates EtOH consumption. Paired t-test showed intraperitoneal administration of GLP-1R agonist, exendin-4, reduced intake (N=8). To elucidate underlying neurocircuitry, excitatory DREADDs were expressed in pancreatic-projecting brainstem vagal motor neurons that regulate insulin release (N=10). Repeated measures two-way ANOVA and unpaired t-tests showed chemogenetic activation reduced insulin sequestration, blood glucose, and EtOH intake. Collectively, these data suggest binge EtOH disrupts insulin signaling to promote subsequent EtOH intake, and that targeting mechanisms to promote insulin restoration, like GLP1R or central circuits regulating insulin release, can reduce EtOH intake.

P217

Role Of Mechanosensation In Modulating Energy Homeostasis

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Living organisms constantly transition between energy states, maintaining a dynamic balance between energy intake through feeding and energy expenditure through physical activity. This homeostatic equilibrium is critical for survival and is regulated by an interplay of chemosensory and mechanosensory feedback from the GI tract. While chemical signals such as leptin and ghrelin, that regulate satiety and hunger have been well studied, the contribution of mechanosensory signals remain underexplored. PIEZO2 is a mechanosensory ion channel essential for transducing mechanical stimuli in both exteroceptive (such as touch) and interoceptive processes, such as baroreflex, bladder fullness sensing, and gut transit. Here, we investigate the role of PIEZO2-expressing neurons in the stomach and duodenum in regulating energy homeostasis using conditional *Piezo2* knockout mice. We found that loss of *Piezo2* in a subset of GI neurons led to increased meal size and reduced voluntary physical activity, indicating disrupted energy homeostasis. Interestingly, consistent with these behavioral changes, *Piezo2*^{cKO} mice also exhibit altered immediate early gene expression in the hypothalamic arcuate nucleus (AgRP and POMC neurons). By uncovering how gastrointestinal mechanosensory signals communicate energy state to the brain, this study will establish a new framework for understanding the regulation of feeding behavior. These insights will not only advance fundamental biology but also open avenues for developing next-generation therapies for obesity and related disorders that can augment existing hormone-based approaches.

P219

A High-Fat High-Sucrose Diet Promotes Hippocampal Neuroinflammation In Male, But Not Female TgF344-Ad Rats

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Alzheimer's disease (AD) neuropathology accumulates for many years during the AD prodrome before the onset of dementia. Neuroinflammation during this prodromal period drives AD progression in regions such as the dorsal hippocampus (dHC). The prodromal period is also when AD patients are vulnerable to the impact of risk factors such as peripheral metabolic impairments (e.g., excess adiposity). We hypothesize that diet-induced dysmetabolism during prodromal AD promotes dHC neuroinflammation and AD-like neuropathology. Prodromal TgF344-AD (Tg) rats and wildtype (WT) littermates (N=65) consumed a control or high-fat high-sugar (HFHS) diet for 11-weeks. A multiplex assay quantified 27 dHC cytokines and ELISAs measured dHC soluble human and rodent amyloid β (A β). Data were analyzed using 3-way ANOVA. Significant interactions with sex were evaluated with 2-way ANOVA (diet genotype) within each sex. EchoMRI confirmed the HFHS diet significantly increased adiposity. Interestingly, dHC cytokines were changed only in male rats. Namely, HFHS-fed males had more dHC IL-4 and EGF than chow-fed males, consistent with evidence that elevated IL-4 and EGF may worsen neuropathology in AD models. The HFHS diet increased interferon- γ levels only in male WT rats, suggesting that a diet-induced compensatory response is absent in male Tg rats. There was a trend for the HFHS diet to increase dHC rodent A β to levels seen in Tg rats. dHC cytokines correlated with rodent but not human dHC A β only in male WT rats, suggesting that dHC A β may have neuroimmune functions. Collectively, these findings indicate that early AD and metabolic disturbances interact to influence neuroinflammation in males but not females.

P220

A Neurotensin Brake On Exploratory Drive Under Persistent Threat

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Exploration is essential for animals to locate food and other necessities in their environment. Avoidance is an adaptive behavior that inhibits exploration when danger is present. Neural circuits that control avoidance by integrating stressful stimuli and modulating exploration remain unknown. Using predator odor (PO) as an innate stressor to induce avoidance in mice, we identified a neural population in the lateral septum (LS) that integrates threat cues and modulates feeding and other exploratory behaviors. 24h after an acute PO exposure (1hr), mice exhibit behavior indistinguishable from controls in the novelty-suppressed feeding (NSF) task and elevated plus maze (EPM). In contrast, 24h after the last exposure, mice exposed to 30d of PO (1hr/day) significantly increase avoidance: increasing feeding latency in the NSF and time spent in the closed arms of the EPM. Calcium recordings in freely exploring mice revealed that LS neurotensin (NT) neurons are responsive to PO. Further, single nuclei RNA-seq analysis shows that among PO-responsive neurons in the LS, NT-enriched inhibitory clusters are

predominant. Chronic chemogenetic activation of LS^{NT} neurons increases avoidance in the absence of PO, while synaptic silencing of LS^{NT} neurons blocks PO-induced avoidance behaviors. Using intersectional genetics, we traced the downstream circuit that encodes PO information to the lateral hypothalamus: chronic, projection-specific activation of LS^{NT}->LHA neurons is sufficient to recapitulate PO-induced avoidance. Finally, we found that neurotensin signaling from the LS is required for PO-induced avoidance. Together, these findings offer a top-down circuit linking psychological stress to avoidance behaviors via limbic system neurotensin signaling.

P221

Adiposity And Sex Modulate Asprosin Expression In Hypothalamic Regions Of Long Evans Rats.

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Asprosin is a fasting-induced adipokine secreted by white adipose tissue that crosses the blood-brain barrier to regulate energy balance. Prior work has established its role in activating orexigenic AgRP neurons in the arcuate nucleus (ARC) and sympathetic circuits in the paraventricular nucleus (PVN) of the hypothalamus. While peripheral and cerebrospinal fluid asprosin levels increase with fasting, it remains unclear whether central asprosin expression is similarly shaped by nutritional state, body composition, or sex. We hypothesized that fasting would increase asprosin in hypothalamic regions of male and female rats, and that this relationship would vary as a function of sex and body composition. Adult male and female Long Evans rats (n=16) were assigned to either a sated or overnight fasted condition. Brains were collected and processed for immunohistochemical detection of asprosin in the ARC, PVN, and dorsal hippocampus (DH), a region increasingly implicated in food intake regulation and responsive to peripheral metabolic signals. Optical density was quantified and analyzed using a 2 x 2 ANOVA (sex x condition). No significant main effects or interactions were observed. However, adiposity positively correlated with asprosin expression in the ARC (r=0.67, p=0.009) and DH (r=0.64, p=0.011), and body weight strongly predicted asprosin in both regions in females (p<0.05). A trend toward higher asprosin in fasted animals was also observed in the PVN. Ongoing work in our lab is examining whether these effects extend peripherally by measuring circulating plasma asprosin and further exploring hormonal influences in females. Together, these preliminary data suggest that body composition and sex are key modulators of central asprosin expression and will inform future studies investigating how energy state shapes hypothalamic circuits involved in appetite and metabolism.

P222

Lithium Orotate Is More Potent Than Lithium Chloride In Conditioned Taste Aversion Learning

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Recently, lithium orotate (LiOr) has been suggested as a therapeutic agent for bipolar disorder (Pacholko 2023) and for Alzheimer's disease (Aron 2025). Orotic acid can act as a carrier to help Li cross cellular membranes more easily and efficiently compared to other salts such as LiCl or Li₂CO₃, with potentially greater bioavailability and capacity to transfer Li to the brain. Therefore, we hypothesized that LiOr would be more potent and induce stronger conditioned taste aversion learning (CTA) compared to LiCl. Adult male Sprague Dawley rats (n=32) were placed on water restriction for 1 week, tapering from 30 min to 15 min daily water. On conditioning day, the rats were given 15 min access to 0.125% saccharin; 15 min later, rats were injected with LiOr or LiCl at either low doses (6 ml/kg of 75mM) or high doses (6 ml/kg of 150mM; n=5-6/group). Control groups were injected with equimolar NaCl. Two-bottle, 24-h preference tests were started the next day between 0.125% saccharin and water, to measure CTA acquisition and extinction (5-21 days). NaCl groups did not form CTAs, with consistently high saccharin preference. High dose LiCl and LiOr groups showed almost complete saccharin avoidance; their CTAs showed little extinction across 21 days. Low dose LiCl and LiOr induced a slightly weaker initial CTA. The low dose LiCl group extinguished rapidly over 4 days. The saccharin preference of the low dose LiOr group, however, remained consistently low over 5 days. Our results show that LiOr can induce a stronger CTA than LiCl. This suggests that even though the low doses had equimolar amounts of Li, the LiOr complex had greater bioavailability than dissociated Li⁺ ions alone. This property may contribute to LiOr's therapeutic efficacy.

P223

Uncovering The Behavioral And Neural Mechanisms Of Food Preference In Diverse Dietary Environments

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Evolutionarily, organisms are poised to prioritize consuming calorically dense foods rich in sugars and fats to promote efficient survival. In modern society, the ready availability of these foods has surpassed this once adaptive strategy. Yet the appetitive nature of fats remains, with a wide variety of fat sources to choose from. Chronic consumption of high-fat diets (HFD) has been demonstrated to induce a robust shift in diet preference, with rodents devaluing their standard diet (SD) via diminished SD consumption even in extreme hunger. However, much of this work has examined only animal-based fats (anim-HFD) and has failed to account for vegetable-based fats (veg-HFD), which have grown greatly in availability. Further, these studies have yet to examine the effects of acute HFD access on shifting diet preference long-term, as well as the neural ensembles driving this shift. Here, we examine the effects of chronic and acute exposure to anim-HFD versus a novel veg-HFD on SD-devaluation. Our results demonstrate that acute and chronic exposure to anim-HFD or veg-HFD leads to similar SD devaluation. Moreover, hypothalamic agouti-related peptide (AgRP) neurons are well-implicated in their role in driving feeding behavior, robustly increasing in activity during a fasted state, and rapidly decreasing activity once food is consumed. It is not yet known how this neuronal population may contribute to driving HFD preference in contexts with varied diets. Preliminary studies are ongoing leveraging in vivo fiber photometry to

examine the role of AgRP neurons across anim-HFD and veg-HFD exposures in hungry versus sated animals. Collectively, these findings offer critical insight into how translationally relevant, diverse fat sources drive maladaptive feeding behaviors.

P224

Inulin-Responsive Vagal Afferent Neurons Are Necessary For The Anorectic Effects Of Inulin Supplementation.

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Obesity is a growing public health crisis, yet current therapeutic strategies remain limited. Therefore, there remains a need to further identify endogenous pathways that regulate satiety and can be therapeutically targeted. Increasing dietary fiber intake is a promising therapeutic approach, as fermentable fibers such as inulin have been shown to reduce food intake and body weight in obesity. Consistent with this, we found that inulin supplemented into a high-fat diet (HFD) significantly reduces cumulative food intake in mice. However, the neural mechanisms underlying fiber-induced satiety remain poorly understood. *We hypothesized that inulin suppresses food intake by activating a discrete population of vagal afferent neurons (VANs) in the nodose ganglia (NG).* Results: To identify inulin-responsive VANs, FosTRAP mice were used to permanently label neurons activated by intragastric (IG) inulin exposure (20%w/v, 100ul/min, 5 min) paired with 4-hydroxytamoxifen administration (30uM, IP). Inulin produced greater TRAP labeling of NG neurons compared to saline, suggesting recruitment of a defined vagal sensory population. To test whether these neurons are required for fiber-induced satiety, mice received bilateral NG injections of a Cre-dependent caspase virus to selectively ablate inulin-responsive VANs. In a within-subject design, mice were exposed to HFD alone and HFD supplemented with 20% inulin. Caspase-mediated ablation attenuated the anorectic effects of inulin supplementation, indicating a role for these neurons in satiety. Conclusion: These findings identify a fiber-responsive vagal afferent population that is necessary for inulin-induced satiety. Targeting this pathway may reproduce the beneficial effects of dietary fiber and inform new therapeutics for obesity.

P225

Hippocampal Encoding Of Meal-Related Cues And Satiety Signals

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Food consumption is shaped not only by metabolic need, but also by prior experience and environmental context relating to food location and availability. Animals must continuously update foraging-based decisions by integrating information about food locations with current internal energy states. The hippocampus, long recognized for its role in spatial and contextual memory, has recently emerged as an important node in the neural circuitry regulating food-seeking, meal-related memory, and energy consumption. To interrogate how hippocampal neurons integrate meal-related spatial memories with internal satiety signals, we used single-neuron calcium imaging with a gradient refractive index (GRIN) lens to monitor neuronal activity in the dentate gyrus of the dorsal hippocampus during a meal-location memory task in rats. We identified neurons that were significantly tuned to spatial areas where food had been previously discovered, suggesting that the dentate gyrus encodes learned representations of meal-associated environments. Furthermore, we observed distinct populations of neurons that were either activated or inhibited upon meal consumption, as well as following intraperitoneal administration of cholecystokinin (CCK), a gut-derived satiation peptide. Longitudinal registration across imaging sessions revealed that a subset of these food- and CCK-responsive neurons also displayed spatial tuning during the meal-location memory task, indicating functional overlap between neural ensembles encoding external food-associated contextual features and internal satiety states. These findings highlight a novel integrative role for hippocampal dentate gyrus neurons in linking memory-guided foraging behavior with metabolic feedback signals.

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From Motivation To Metabolism: A Neural Circuit Modulating Feeding Behavior

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Obesity remains a major global health crisis, with limited efficacy and tolerability of current pharmacological treatments underscoring the need for novel neurobiological targets. Feeding behavior arises from integration of homeostatic and reward processes mediated by the lateral hypothalamus (LH) and nucleus accumbens (NAc), yet the circuit mechanisms linking these structures remain poorly understood. Accumulating evidence suggests that dopamine signaling via the NAc modulates hypothalamic feeding centers, but the intermediate pathways remain undefined. We hypothesize that dopamine D2 receptor-expressing medium spiny neurons (D2R-MSNs) in the NAc inhibit food intake via a polysynaptic glutamatergic relay through the ventral pallidum (VP) to the LH (NAc→VP→LH). Adult male and female mice (C57BL/6J, Adora2A-Cre, vGLUT2-Cre, vGAT-Cre; n≈12/sex per study) were used. Viral-genetic circuit tracing (cTRIO) mapped projections from NAc D2R-MSNs through the VP to the LH, identifying glutamatergic VP neurons as relay nodes. To assess function, chemogenetic inhibition (DREADDs) was applied to NAc→VP projections, and feeding was quantified using home-cage metabolic monitoring. Statistical analyses included ANOVA with Bonferroni correction and repeated-measures ANOVA. Tracing studies indicate that NAc D2R-MSNs selectively target VP glutamatergic neurons projecting to the LH, and chemogenetic inhibition of NAc→VP terminals suppresses feeding. These findings define a previously uncharacterized NAc→VP→LH circuit integrating reward and homeostatic control of feeding and identify novel targets for treating compulsive overeating and obesity refractory to current therapies.

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Unmasking Mouse Appetite: A Mass&Ndash;Metabolism Approach To Precise Food Intake Quantification

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Accurate measurement of food intake in mice remains a major technical challenge due to inconsistent feeding behaviors and the well-recognized discrepancy between food removed from a feeder and food actually consumed. Automated feeding systems offer high resolution measurements of individual feeding events, but cannot distinguish true consumption from spillage, hoarding, or grooming related losses—issues that are especially prominent with high fat, crumbly diets. Modern indirect calorimetry systems simultaneously record energy expenditure and continuous body mass, creating an opportunity to integrate these physiological readouts to improve intake estimation. We present an automated analytical framework that combines energy intake, metabolic rate, and dynamic body mass changes to generate a more accurate estimate of true food consumption. By applying principles of energy balance and demonstrating the limits on the maximum possible intake rate, we use observed mass fluctuations and measured energy expenditure to infer consumption at the level of individual feeding events. This approach corrects for spillage related error, reduces noise in longitudinal feeding datasets, and improves statistical power when comparing intake between groups. Integrating mass change and metabolic rate with feeding records substantially increases the fidelity of intake estimates relative to feeder-based measurements alone. The method enhances data quality, can be applied retroactively to existing high granularity datasets, and provides the research community with a standardized tool for more precise phenotyping of energy balance and feeding behavior in mouse models.

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Evidence Of Persistent Hunger Following Dietary Weight Loss In MiceFrankie/D Heyward^{1,2,3,4,5}, Evan/D Rosen^{3,4,5}

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Rationale: Over 40% of U.S. adults live with obesity, and nearly half have attempted weight loss, yet most efforts result in weight regain. Rodent models have been used to study the physiological drivers of this phenomenon, but it remains unclear whether they recapitulate susceptibility to weight regain after sustained weight loss. Hypothesis: Mice with prior diet-induced obesity remain susceptible to weight regain following sustained weight loss. Species: Mouse (*Mus musculus*). Number of Subjects: 50 male mice in Experiment 1; 72 male mice in Experiment 2. Procedures: In Experiment 1, male mice were rendered diet-induced obese by 16 weeks of high-fat diet feeding, then calorically restricted (CR) to induce weight loss. Food intake was assessed after CR. In Experiment 2, diet-induced obese mice were calorically restricted until weight-matched to controls, then pair-fed for 0, 8, or 28 days, or chronically. Upon return to ad libitum feeding, food intake and body weight regain were assessed. Results: In Experiment 1, mice with prior diet-induced obesity exhibited marked hyperphagia after CR. In Experiment 2, all reversed dietary obesity (ReDO) groups displayed persistent hyperphagia relative to controls and chronically pair-fed mice. Variability in body weight regain among pair-fed ReDO mice correlated with initial 4-week weight gain on high-fat diet. Conclusions/Relevance: These findings establish ReDO as a mouse model for mechanistic studies of weight loss-associated hyperphagia and weight regain, and identify early diet-induced weight gain as a potential predictor of regain susceptibility.

P229

Contribution Of Cephalic Phase Insulin Release To Glucose Regulation In Humans

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Cephalic phase insulin release (CPIR) is a rapid, neurally mediated insulin response triggered by sensory cues at meal onset, priming the body to manage incoming glucose efficiently. Our previous work shows that oral stimulation with glucose, maltodextrin, and other sweeteners elicits CPIR, but its presence and magnitude vary greatly across individuals. In rodents, CPIR improves glucose tolerance by limiting postprandial hyperglycemia. Evidence in humans, however, remains limited and inconsistent. We hypothesize that CPIR also improves glucose control in humans, but that chronic use of non-nutritive sweeteners (NNS) attenuates CPIR due to metabolic prediction errors, which in turn negatively impact glucose tolerance. We are currently conducting a study examining CPIR and glucose regulation in habitual NNS users and non-users. Following a standardized evening meal and overnight fast, participants complete a modified oral glucose tolerance test. After catheter placement and a 15-min rest, four baseline blood samples are collected. At time 0, participants consume 300 mL of a fruit flavored beverage containing 75 g glucose over 5 min. Blood samples are collected at 2, 4, 6, and 8 min (cephalic period) and at 15, 30, 45, 60, 90, and 120 min (postprandial period). Plasma glucose, insulin, C-peptide, and pancreatic polypeptide are assayed. Linear mixed-effects models will assess group differences in CPIR (Δ and AUC for C-peptide and insulin), with time and group as fixed factors and subject as a random factor. Associations among NNS use, CPIR, and glucose tolerance will be examined using regression models. Preliminary data look promising. Study findings will confirm the role of CPIR in human glucose regulation and whether habitual NNS use interferes with this process.

P230

Circadian Alignment And Feeding Predictability Mediate The Metabolic Efficacy Of Calorie Restriction

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The metabolic benefits of calorie restriction (CR) are traditionally attributed to a simple energy deficit. However, CR introduces three variables: caloric load,

prolonged daily fast, and a habitual feeding schedule. Because food is a dominant synchronizing cue, this unique feeding pattern may be an obligatory temporal condition to elicit full benefits of CR. We hypothesize that CR efficacy relies on the habitual feeding-fasting cycles to form an adaptive metabolic memory that primes biochemical pathways ahead of nutrient influx to optimize metabolic efficiency. Male C57BL/6J mice (n=24/group) were placed on 5 paradigms: *ad libitum* (AL); 30% CR fed consistently at active phase onset (ZT 12; CR-12) or inactive phase (ZT 6; CR-6); and sporadic CR alternating mealtimes around ZT 12 (CRS-12) or ZT 6 (CRS-6). Indirect calorimetry, body composition, and glucose/insulin tolerance were assessed. Repeated-measures ANOVA evaluated tolerance, RER, and body composition; ANCOVA was used to assess energy expenditure. When feeding was aligned with the active phase, CR-12 group consolidated intake (~2 hours), displayed dynamic fuel switching (RER ~0.7-1.0) and diminished fat mass accrual. Disrupting this predictability (CRS-12) abolished intake consolidation, blunted RER amplitude, lowered insulin sensitivity, and increased fat mass accrual despite identical caloric deficits. Furthermore, shifting feeding to the inactive phase (CR-6, CRS-6) eliminated intake consolidation entirely. Consequently, despite 30% deficits, both ZT 6 groups accrued fat similarly to AL controls. Therefore, an absolute energy deficit does not guarantee improved health. The metabolic benefits of CR are contingent upon the consistent temporal organization of feeding and its alignment with endogenous rhythms.

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Characterization Of Signaling Pathway-Selective Ghrelin Receptor (Ghsr) Mouse Models To Guide Drug Development

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Ghrelin is an orexigenic gut hormone that regulates energy balance and glucose homeostasis via the growth hormone secretagogue receptor (GHSR). The GHSR exhibits high constitutive activity, LEAP2-mediated inverse agonism/antagonism, and pathway-selective signaling via G proteins and β -arrestin (β arr). We identified a conserved motif in intracellular loop-2 (ICL2) that biases GHSR signaling between G proteins and β arr, prompting our hypothesis that GHSR physiology is signaling pathway-dependent. To test this, we genetically engineered mice with GHSR-ICL2 point mutations that bias signaling towards the G protein (GHSR^{Gprot}) or β arr (GHSR ^{β arr}) pathway. In vitro analyses confirmed complete agonist-induced signaling bias, albeit with opposing effects on surface expression and proportionally reduced constitutive G α q activity in the GHSR^{Gprot} mutant. Preliminary in vivo evaluation showed that chow-fed, female GHSR ^{β arr} mice exhibit lower body weight, moderately increased fat oxidation, and improved glucose control despite normal energy intake and energy expenditure. GHSR^{Gprot} mice were largely similar to WT littermates except for modest reductions in male body weight, body length, and plasma IGF-1. Acute GHSR agonist-induced hyperglycemia and hyperphagia were abolished in chow-fed male and female GHSR ^{β arr} mice, while these responses were sex-dependent in GHSR^{Gprot} mice. On a high-fat diet (HFD), female GHSR ^{β arr} mice maintained normal body weight gain despite reduced metabolic efficiency and the retention of improved glucose tolerance, whereas HFD-fed GHSR^{Gprot} mice were similar to controls. These models provide unique tools to dissect pathway-selective GHSR metabolic physiology and may support the rational design of biased GHSR therapeutics.

P232

Body Fat Associates With Nocturnal Sleep Macro-Architecture In Young Adults

Daphne I Valencia¹, Daniel A R Cabral¹, Caroline Chovanes¹, Sue A Shapses², Andrea M Spaeth¹

¹Department of Kinesiology and Health, Rutgers University, New Brunswick, NJ, United States, ²Department of Nutritional Sciences, Rutgers University, New Brunswick, NJ, United States

Insufficient sleep is associated with excess body fat and daytime sleepiness in adults. Prior work has shown that body fat is negatively associated with time spent in non-rapid eye movement (NREM) stage 3 sleep and positively associated with sleep fragmentation. Findings related to REM sleep have been mixed. Here we focused on young adults, who are at increased risk for insufficient sleep. We hypothesized that body fat would be associated with less time in NREM stage 3 sleep and more wake after sleep onset. Participants were 74 students enrolled at a public university (20 $\pm$ 2y; 60% female) who wore an actigraph on their non-dominant wrist 24/7 for 14 days and completed at-home polysomnography (PSG) on a night of typical sleep. Body composition was measured by dual X-ray absorptiometry. Pearson's and Spearman's correlations were used to identify significant associations followed by general linear models controlling for sex. As fat mass increased, sleep efficiency decreased (b=-0.0007, p=0.02), and time spent in NREM stages 1 and 3 decreased (b=-0.004, p=0.045, b=-0.018, p=0.01). Visceral adipose tissue associated with NREM stage 3 latency and duration such that individuals with more visceral adiposity took longer to enter their first bout of NREM stage 3 sleep (b=4.853, p=0.02) and spent less time in NREM stage 3 across the night (b=-0.499, p=0.014). Findings contribute to evidence demonstrating bidirectional relationships between sleep health and body composition. Individuals with excess adiposity are at risk for chronic inflammation and neuroendocrine changes that may disrupt sleep. Disruptions in sleep, such as less time spent in slow wave sleep and sleep fragmentation may lead to alterations in hormones (i.e., growth hormone) that affect energy balance and metabolism.

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The Influence Of Semaglutide On The Intrinsic Excitability Of The Olfactory Bulb

Rimil Guha Roy^{1,2}, Saptarsi Mitra^{1,2}, Giorgio Belperio^{1,2}, Debra A Fadool^{1,2,3}

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Approximately 15 million patients in the USA have taken semaglutide (sema), a glucagon-like peptide-1 receptor agonist (GLP-1RA) to combat diabetes and

unwanted weight gain Herein, we used wildtype and transgenic mice to map the targets of GLP-1 signaling In the olfactory bulb (OB) that remains less explored despite GLP-1R being present on the mitral and tufted cells (M/TCs), which are its principal output neurons. Bath application of sema significantly increased the evoked action potential firing frequency ($p=0.0203$) and lowered the rheobase ($p=0.0406$) in recorded M/TCs from in vitro OB slices patch-clamped in the whole-cell configuration. The enhanced excitability was driven by a significantly decreased interspike interval across suprathreshold current steps ($p=0.0109$). To validate in vivo access to sema, mice were intraperitoneally injected with either FITC-conjugated or untagged sema. Within 4 hours of sema treatment, induction of c-fos was observed in the OB, nucleus tractus solitarius, and area postrema, and was absent in that of GLP-1R-null mice. A separate cohort of mice maintained on either control or moderately high-fat diet, and treated daily with sema for 1-month duration were examined for changes in metabolic and ingestive behaviors. Sema-treated obese mice showed reduced daily food intake with longer but less frequent meals during the dark cycle, and increased lipid metabolism when compared to saline-injected animals. The degree of sema-induced weight loss was independent of diet, however, an isocalorically-restricted group (yoked to sema weight loss) lacked rebound weight gain post-treatment compared to that of sema-treated mice. Our results demonstrate the presence of semaglutide-induced signaling in the OB that may alter odor-driven feeding behavior.

10:00 - 11:30 AM	Regency B
Symposium 2: Boldly Going: The next generation in testing neuromodulators	

Chair(s): Kyle Burger

10:00

Monoamine Release Dynamics In The Human Amygdala Dissociate Components Of Food Reward

Matt Howe^{1,2}, Seth Batten¹, Leonardo Barbosa¹, Monica Ahrens³, Terry Lohrenz¹, Jason White¹, Robert Bina⁴, Mark Witcher^{1,5}, Read Montague^{1,6}, Alexandra DiFeliceantonio^{1,7}

¹Fralin Biomedical Research Institute at Virginia Tech, Roanoke, VA, United States, ²School of Neuroscience, Virgi, Blacksburg, VA, United States, ³University of Kentucky Medical Center, Kansas City, KS, United States, ⁴Department of Neurosurgery, Banner University Medical Center , Phoenix, AZ, United States, ⁵Department of Neurosurgery, Virginia Tech Carillion School of Medicine, Roanoke, VA, United States, ⁶Department of Physics, Virginia Tech, Blacksburg, VA, United States, ⁷Department of Human Nutrition, Foods, and Exercise, Virginia Tech, Blacksburg, VA, United States

The decision-making process that drives food choice can potently modify overall health and disease risk. Studies, largely conducted in rodents, have underscored the importance of reward-related signals in the brain for guiding food choice. These signals can override homeostatic ones, and likely contribute to the ability of energy dense, highly palatable foods to drive poor health outcomes in humans. While many brain circuits have been implicated in the control of such reward-based eating, there is a growing consensus that it is steered by monoamine (dopamine, serotonin, and norepinephrine) release in brain areas like the amygdala. However, many of the key findings that support these ideas have yet to be translated to humans, due in large part to the lack of technologies that enable insights into the temporal dynamics of monoamine release in the human brain that are comparable to those provided by tools optimized for rodents. Recently, our group has been engaged in an effort to bridge this translational gap through the development of an approach that affords sub-second, concurrent detection of all monoamines in the brain of conscious humans. Here, we present results from on-going studies using this approach to study how monoamine neurotransmitter release in the human amygdala is modulated by food-predictive cues (n=10), as well as the valence of primary food rewards (n=8). Our data support a model whereby dopamine and serotonin signal food valence and cue-reward associations through unique patterns of opponent release. Collectively, these findings represent a first-of their kind test of the translatability of key findings from animal models and identify signatures of neurotransmitter release that may ultimately underwrite both adaptive and maladaptive food choices.

10:30

Control Of Ingestion By The Caudal Brainstem

Zachary Knight

University of California, San Francisco, San Francisco, CA, United States

The passage of food through the alimentary canal generates a series of feedback signals that are sensed by the brain and used to control feeding behavior. Many of these signals converge on the caudal brainstem, which contains the key neural circuits that drive meal termination. I will describe our work investigating the dynamics and function of these circuits during ingestion. A central theme is that these circuits control behavior by integrating layers of feedback signals from the mouth and gut. These feedback signals influence behavior both in real-time during ingestion and over longer timescales through learning.

11:00

Monoamine Recordings In Healthy Humans During Social Exchange And Ingestion

Read Montague

10:00 - 11:30 AM	Millennium Hall
Oral Session 4: K-Pop Diet Hunters: Diet Quality & Health	

Chair(s): Emily Noble

10:00

Genetic Architecture Of Ultra-Processed Food Consumption Links Neurodevelopmental And Metabolic Pathways To Habitual Diet

Filip Morys^{1,2}, Daiva E. Nielsen³, Lang Liu^{1,4}, Arsene Kanyamibwa⁵, Atheer Attar³, Tongzhu Meng³, Mari Shishikura¹, Annette Horstmann⁵, Alain Dagher¹

¹Montreal Neurological Institute, McGill University, Montreal, QC, Canada, ²Modern Diet and Physiology Research Center, Montreal, QC, Canada, ³School of Human Nutrition, McGill University, Montreal, QC, Canada, ⁴Department of Human Genetics, McGill University, Montreal, QC, Canada, ⁵Department of Psychology, Faculty of Medicine, University of Helsinki, Helsinki, Finland

Ultra-processed food (UPF) consumption is rising globally and is implicated in non-communicable diseases including cancer, metabolic disorders, and dementia. Engineered to optimize palatability, UPFs introduce sensory and metabolic properties that may drive consumption beyond that of traditional foods. Given that

food preferences are heritable, UPF consumption may similarly reflect an underlying genetic architecture - yet this remains unexplored. Here, we present a genome-wide association study of UPF consumption in over 142,000 UK Biobank human participants with a polygenic score validation in an independent cohort. SNP-based heritability analysis revealed that UPF consumption is heritable ($h^2 = 6.06\%$). We identified 15 genome-wide significant loci ($p < 5 \times 10^{-8}$) mapping to 23 genes, most of which cluster within two major chromosomal inversions - 17q21.31 and 8p23.1 - linked to brain development and morphology, as well as FGF21, a gene associated with sugar and alcohol preference. A polygenic score derived from these associations significantly predicted UPF consumption in an independent validation cohort ($n = 7,149$, $\beta = 0.59$, $p = 0.0002$). Downstream analyses using Functional Mapping and Annotation of Genome-Wide Association Studies showed that UPF-associated genes are preferentially expressed in neurons and oligodendrocyte precursor cells of subcortical brain regions previously implicated in UPF intake. Significant genetic correlations with metabolic traits (fasting insulin, insulin resistance, blood lipid levels), anthropometrics, macronutrient intake, educational attainment, and self-control further highlight the broad physiological and behavioral mechanisms of UPF consumption. These findings reveal a neurobiological architecture underlying UPF intake with implications for diet-related disease prevention.

10:15

High-Fat Diet Remodels Vagal Sensory Pathways Through Inflammation To Promote Hyperphagia

Isadora Braga^{1,2}, Laryssa Oliveira Coutinho¹, Alan de Araujo^{1,2}, Rebeca Mendez^{1,2}, Claire de La Serre³, Dan Brierley⁴, Guillaume de Lartigue^{1,2}

¹Monell Chemical Senses Center, Philadelphia, PA, United States, ²University of Pennsylvania, Philadelphia, PA, United States, ³Colorado State University, Fort Collins, CO, United States, ⁴University College London, London, United Kingdom

Vagal sensory neurons send meal-related signals from the gut to the brain to limit food intake. We previously found that short-term high-fat diet (HFD) rapidly causes vagal fiber withdrawal and impaired satiety, suggesting that peripheral sensory remodeling may drive overeating. We hypothesized that HFD induces inflammation-dependent vagal remodeling that disrupts gut-brain signaling. **Methods:** Vagal structure and nutrient-evoked NTS cFos were assessed in HFD-fed mice. **Results:** To test whether vagal remodeling is secondary to hyperphagia or triggered by diet itself, we pair-fed mice HFD to match chow-fed caloric intake. Despite matched intake, HFD reduced vagal fiber density and nutrient-induced NTS cFos, indicating that diet composition drives vagal remodeling and impaired gut-brain signaling ($n=5/\text{group}$, $p=*$). Because HFD causes low-grade inflammation, we gave the NSAID flurbiprofen twice daily during the first 3 weeks of HFD feeding. Flurbiprofen prevented vagal remodeling, preserved nutrient-induced NTS cFos ($n=5/\text{group}$, $p=*$), and blocked hyperphagia and excess weight gain ($n=12/\text{group}$, $p=***$), identifying inflammation as a key driver. Caloric restriction, diet reversal, and semaglutide failed to restore vagal structure or function, but VSG rescued both ($n=6/\text{group}$, $p=*$). Chemogenetic activation of NTS neurons suppressed food intake in HFD-fed mice ($n=8/\text{group}$, $p=***$), indicating that downstream circuits remain functional despite impaired vagal input. **Conclusion:** HFD induces inflammation-dependent remodeling of vagal sensory pathways independent of excess caloric intake, disrupting gut-brain satiety signaling and promoting hyperphagia. This defect originates in peripheral sensory pathways and is reversed by interventions that more broadly normalize the gut environment.

10:30

Methods Of Coding Food Into Nova Food Classes: Interrater Reliability Between A Reproduced Machine Learning Algorithm With Manual Coding

Laura Claire Walker^{1,2}, Amelia Blumberg^{1,3}, Eunice Chen¹

¹Psychology and Neuroscience, Temple University, Philadelphia, PA, United States, ²Winston Center on Technology and Brain Development, University of North Carolina at Chapel Hill Department of Psychology and Neuroscience, Chapel Hill, NC, United States, ³Ferkauf Graduate School of Psychology, Yeshiva University, New York, NY, United States

Rationale: Categorizing the degree to which food is processed is challenging. The NOVA food system groups food into 4 classes: (1) unprocessed/minimally processed foods, (2) processed culinary ingredients, (3) processed foods, and (4) ultraprocessed foods. Menichetti et al., (2023) developed a machine learning algorithm (MLA) to categorize foods into NOVA classes given their nutrient content. Researchers have also categorized food into NOVA classes using manual coding of nutrition food codes. Hypothesis: We hypothesized that there would be agreement between a reproduction of the MLA with and manual coding of NOVA classes. Methods: 24-hour food intake data was collected in-person in person for 105 healthy college students using the ASA24 Dietary Assessment Tool, 2024 (NCI, 2024) resulting in 2078 food items. The MLA (Menichetti et al., 2023) to categorize food into NOVA classes was reproduced (LCW); and items were manually categorized into NOVA classes (AB). Cohen's κ was used to assess interrater reliability between the MLA coding and manual coding for each of the foods and drinks consumed, and for the average %s of total energy intake of each NOVA class for each participant. Results: Interrater reliability between the 2 methods for classifying NOVA classes for each food and drink item was $\kappa=.63$; for NOVA class 1, $\kappa=.39$; for NOVA class 2, $\kappa=.56$; for NOVA classes 3 and 4, respectively $\kappa=.13$ and $.12$. All findings were significant ($p < .0001$), with bootstrapping (1000 resamples) indicating stability. Conclusions: Interrater reliability for each food and drink item coded was substantial; moderate for NOVA class 2, fair for NOVA class 1, but slight for NOVA classes 3 and 4. These differences may be reflective of the distinct data types used by each method for classification.

10:45

Effects Of Controlled Diets High In And Free Of ULtraprocessed Food On The Brain Of Emerging Adults

Emma Leslie¹, Maria Rego², Monica Ahrens³, Wenjing Yu², Mary Elizabeth Baugh¹, Anastasia Groccia⁴, Rhianna Sullivan¹, Han Lee¹, Ryann Kolb¹, Delbert Herald¹, Valisa Hedrick², Kevin Davy², Benjamin Katz⁵, Brenda Davy², Alexandra DiFeliceantonio¹

¹Fralin Biomedical Research Institute at Virginia Tech, Roanoke, VA, United States, ²Department of Human Nutrition, Foods, and Exercise at Virginia Tech, Blacksburg, VA, United States, ³Department of Internal Medicine, Division of Medical Informatics, Kansas City, KS, United States, ⁴School of Neuroscience at

The average American consumes 55% of their daily energy from ultraprocessed foods (UPF), which are created through industrial processes and contain additives not used in home kitchens. Emerging evidence links UPF consumption with adverse health outcomes including overweight and obesity, metabolic disease, and cancer. Adolescents are in a critical period for brain maturation and consume more UPFs than other age groups. Here, we aim to investigate if a diet high-in UPF alters brain response to a milkshake compared with a diet free-from UPF. In a crossover, randomized controlled trial participants (n=22) aged 18-25 completed two, 2-week controlled feeding periods including a UPF (81% UPF) diet and a NonUPF (0% UPF) diet. Before and after each diet intervention participants consumed a milkshake concomitant with functional magnetic resonance imaging (fMRI). Orbitofrontal cortex (OFC; [16, 28, -28], T=4.74, SVC pFWE = 0.033) response to milkshake receipt decreased after the UPF diet and increased following the NonUPF diet in adolescents (aged 18-21 years) but not young adults (aged 22-25 years). We next examined if change in brain response predicted intake and observed that entorhinal cortex ([-20 -8 -38], T=6.01, pFWE = 0.002 and [20 -6 -36], T=5.24, pFWE = 0.002) activity in response to milkshake consumption predicts intake at a subsequent ad libitum buffet regardless of the diet intervention or age. Entorhinal cortex receives projections from many areas previously demonstrated to predict intake. This work demonstrates UPF consumption may preferentially alter brain response to palatable foods in younger people.

11:00

A Western Diet Alters The Mitochondrial-Associated Transcriptome And Impairs Mitochondrial Bioenergetics In The Hippocampus Of Cognitively Impaired Mice (New Investigator Travel Awardee)

Ana L Loera-Lopez^{1,2}, Junwon Heo³, Magen N Lord², David L Miller^{3,4}, Jessica R Hoffman², Anson D Sing⁵, Tianyi Zhang⁶, Alexia King⁵, Eugene F Douglass⁷, Luke J Mortensen^{4,6}, Steven A Sloan⁵, Jarrod A Call^{1,3,4}, Emily E Noble^{1,2}

¹Neuroscience Graduate Program, Athens, GA, United States, ²Department of Nutritional Sciences, Athens, GA, United States, ³Department of Physiology and Pharmacology, Athens, GA, United States, ⁴Regenerative Bioscience Center, Athens, GA, United States, ⁵Department of Human Genetics, Emory, GA, United States, ⁶School of Chemical, Materials, and Biomedical Engineering, Athens, GA, United States, ⁷Pharmaceutical and Biomedical Sciences, Athens, GA, United States

Consuming diets high in saturated fats and added sugars, termed a Western diet (WD), is associated with cognitive impairment and neurodegenerative disease. Hippocampal-dependent cognitive functions are susceptible to both a WD and mitochondrial dysfunction. We hypothesized that a WD would alter mitochondrial bioenergetics in the hippocampus. C57BL/6J mice (total n=84) fed a WD, but not their chow-fed counterparts, displayed impaired hippocampal-dependent spatial memory in the Novel Location Recognition task (one sample t-test against chance levels). We conducted RNA sequencing of hippocampal neurons to elucidate transcriptomic changes related to mitochondrial functions followed by Virtual Inference of Protein-activity by Enriched Regulon (VIPER) analysis to predict changes to transcription factor (TF) activities. Finally, we measured mitochondrial function (i.e. respiratory conductance, enzyme activity, and antioxidant buffering capacity [AOxBC] of reactive oxygen species [ROS]). Statistical significance for gene expression data was defined as $\log_2\text{FoldChange} > 1$ and $p(\text{adj}) < 0.05$ and by Welch's t-test $p < 0.05$ for all other comparisons. Our results revealed a downregulation of all protein-encoding genes on mitochondrial DNA and of pathways related to mitochondrial complex I (MCI) in WD-fed mice. A WD also impaired MCI-based respiratory conductance and enzyme activity in hippocampal tissues. These findings were associated with a fragmented mitochondrial network, elevated ROS, and reduced AOxBC. Our VIPER analysis predicted decreased activity of TFs governing neural excitability. We conclude that WD consumption interferes with processes underlying mitochondrial bioenergetics in the hippocampus and provides insight into how a WD may contribute to cognitive dysfunction.

Prebiotic Supplementation Mitigates High-Fat Diet-Induced Disruption Of Estrous Cyclicity And Alters The Vaginal Microbiome.Julia Cook¹, Jennifer Houston¹, Zowi Pogonat-Walters¹, Maja Legatt¹, Kellie Tamashiro², Claire de La Serre¹¹Colorado State University, Fort Collins, CO, United States, ²Johns Hopkins University, Baltimore, MD, United States

Consumption of a high-fat (HF) diet has profound effects on female fertility, although the mechanisms underlying these effects remain poorly understood. There is evidence that diet can modulate the vaginal microbiome and disruption of the vaginal microbiome has been linked to increased susceptibility to infection and other adverse reproductive outcomes. In this study, we assessed the impact of HF feeding on reproductive health, using female Wistar rats (n = 6) fed either chow, HF (45% kcal from fat) or HF supplemented with prebiotic (resistant starch, RS) diets. HF diet consumption altered vaginal microbiome composition, including depletion of *S.Marmotae* compared to chow fed animals. HF-fed females also showed greater susceptibility to vaginal infection compared to chow fed females (p < 0.05), measured by the number of days exhibiting infection patterns on estrous cytology slides and exhibited significantly increased estrous cycle length, indicating disrupted cyclicity. Prebiotic supplementation in HF fed females mitigated these effects, restored normal cycling patterns and reduced infection duration. Importantly, these changes occurred in the absence of detectable differences in body weight or alterations in gut to brain signaling, suggesting that female reproductive outcomes may be particularly sensitive to HF diet exposure even in the absence of typical metabolic or neural changes. Together, these findings support a model in which HF diet disrupts estrous cyclicity in association with vaginal microbiome remodeling, while prebiotic supplementation may provide protection against these effects.

11:30 - 1:00 PM	On Own
Lunch on Own	

11:30 - 1:00 PM	Lescaze
Elsevier Meeting (Invitation Only)	

11:45 - 12:45 PM	Regency B
New Investigator Event - Professional Development Panel - What is Next After Grad School?	

Join scientists from academia, industry, and government for a live Q&A about career paths, job searching, networking, and what makes an applicant competitive. Complimentary lunch will be available to the first 30 attendees on a first-come, first-served basis.

[Register Here.](#)

1:00 - 2:00 PM	Millennium Hall
Mars Lecture 2: Randy Seeley	

Chair(s): Amber Alhadeff

1:00

To Be GIP Or Not To Be GIP, That Is The Question

Randy Seeley

University of Michigan

The advent of polyagonists has opened up tremendous new avenues for the pharmacological treatment of obesity. Numerous different combinations are being actively investigated. The gut hormone GIP and its associated receptor are active targets for polyagonists such as tirzepatide and retatrutide that demonstrate superior weight loss to GLP-1R agonists alone. These clear successes belie a dilemma. Reduced GIP receptor activity is associated with resistance to weight gain in mice and relative leanness in humans. Such genetic analyses support the notion that antagonizing the GIP receptor might be an appropriate strategy for weight loss medications. Maritide is a polyclonal antibody that serves as a GIP antagonist conjugated with two GLP-1 agonist peptides. In both pre-clinical and clinical data, maritide also leads to significant weight loss. How can we understand drugs that have the opposite effect on the GIP receptor, both being effective therapeutic strategies? This presentation will review a wide range of preclinical data to explore the underlying neural circuits for the actions of these drugs and explore the potential hypotheses that might resolve the dilemma presented by GIP.

2:15 - 4:30 PM	Millennium Hall
NITA Symposium	

Chair(s): Matt Hayes

2:15

Experimental Induction Of Uncertainty About Food Availability Over Two Weeks Impacts Brain, Behaviour, And Cognition In Humans. (Elsevier Physiology & Behavior New Investigator Travel Awardee)

Justin J Sung¹, Natasha Mattar¹, Noemie Saulnier¹, Laure Chaboussant¹, Filip Morys², Dana M Small^{1, 2, 3}

¹McGill University, Montreal, QC, Canada, ²The Neuro, Montreal, QC, Canada, ³Northwestern University, Evanston, IL, United States

Food insecurity (FI) affects around 700 million people world-wide and is linked to obesity, cardiovascular disease, and all-cause mortality. Animal models show that FI increases food intake, alters dopamine signaling, cognition and metabolism. Whether this translates to humans is unknown; however, epidemiological studies support this possibility and show that even “mild” FI – characterized as the experience of uncertainty in accessing sufficient food – leads to considerable

negative health outcomes. Here we develop a novel paradigm to manipulate food uncertainty in healthy adults by varying food provision between 10% and 40% of estimated daily total energy expenditure over a 15-day experiment claiming to study the effects of food intake on cognition (n=15, 8 female and ongoing). Brain response to milkshake, impulsivity, risk tolerance, and ad libitum buffet meal intake was measured pre and post 6 lab days wherein participants underwent cognitive testing before and after a variable sized meal. Following the manipulation participants reported feeling uncertain whether the amount of food provided would be enough ($\mu=31.5$, anchored 0= “not certain at all”, 100= “more certain than anything”). As predicted, the intervention increased ad libitum intake ($p<0.001$), produced a trending increased risk tolerance ($p=0.06$) and trending decrease in ventral striatal response to milkshake ($pSVC=0.09$). In addition, response in dorsolateral prefrontal cortex correlated positively with rated induced uncertainty ($pFWE=0.03$). This work provides preliminary support that food uncertainty can be experimentally manipulated in humans and that the experience may produce similar effects as observed in animal models. Data collection, including a control group with non-variable meals, is ongoing.

2:30

Early-Phase Ingestive Microstructure As A Behavioural Marker Of Semaglutide Response In Obesity: An Interim Analysis Of The Digrat Study (New Investigator Travel Awardee)

Michele Serra^{1,3}, Ahmed Al-Humadi², Werd Al-Najim², Daniela Alceste³, Nicole Jucker^{1,3}, Marco Bueter³, Carel le Roux²

¹Department of Endocrinology, Diabetology and Clinical Nutrition, University Hospital Zurich, Zurich, Switzerland, ²Diabetes Complications Research Centre, Conway Institute, University College Dublin, Dublin, Ireland, ³Department of Visceral Surgery, Hospital Maennedorf, Maennedorf, Switzerland

Current monitoring of GLP-1 receptor agonist therapy in obesity relies largely on body weight and may miss early treatment-related adaptation. We hypothesised that semaglutide induces early measurable changes in ingestive behaviour before longer-term clinical outcomes fully emerge, and that direct assessment of these adaptations may have future value for treatment monitoring in clinical practice. Adult females with obesity (BMI>30) initiating semaglutide (n=43) were studied alongside controls with untreated obesity (n=25) and controls with normal-weight (n=35). After an overnight fast, ingestive behaviour during consumption of a standardized liquid test meal was recorded under standardised conditions using a drinkometer and complemented by clinical assessments and visual analogue scales. Measurements were obtained at baseline and repeated follow-up visits after dose escalation. Interim analyses used non-parametric between-group comparisons and exploratory longitudinal models adjusted for baseline values and weight loss. Baseline macrostructural and microstructural ingestive parameters were largely comparable across cohorts with obesity. Semaglutide treatment was associated with improvements in body weight and adiposity. Behavioural changes were detectable early after treatment initiation and were most evident in burst-dependent ingestive measures, particularly during the first burst and early phase of the meal, whereas later intake phases and higher-order burst organisation showed alterations related to satiation. These interim findings support the feasibility of measuring ingestive behaviour to detect early treatment-related adaptation during semaglutide therapy and suggest potential value for mechanistic phenotyping and future clinical monitoring in obesity care.

2:45

Integrating Internal And External Signals To Optimize Food Decision Making

Yige Sun, Ahmed Bouteldja, Justin Sung, Zheyi Li, Filip Morys, Dana Small
McGill University, Montreal, QC, Canada

It is now well recognized that post-oral signals drive food reinforcement with distinct pathways associated with post-oral reinforcement for fat and carbohydrate. In the current study, we asked whether the type of fuel being used (i.e., nutrient partitioning) influences the reinforcement value of that fuel. In other words, when your body uses carbohydrates as a fuel, does this change how you value fatty or sugary foods? 28 participants with a healthy weight underwent fMRI-compatible indirect calorimetry (IC-fMRI) to estimate fuel use and performed an auction task to assess food reinforcement in the fMRI scanner. The type of fuel being used was determined by calculating the respiratory quotient (RQ) with a value of .7 reflecting fatty acid oxidation and a value of 1 reflecting glucose oxidation. In the food auction task, participants bid against a computer for the opportunity to eat foods comprised primarily of fat, carbohydrate, or their combination. Bid amount provided our measure of reinforcement value. A linear mixed-effects model including RQ, macronutrient category, their interaction, BMI, sex, age, and liking, with random intercepts for subject and food item, was performed to determine if fuel use was associated with food value. A significant RQ $\times$ macronutrient interaction emerged ($\beta = 1297.79$, $p = .009$), indicating that the relationship between fuel use and fuel value differed as a function of macronutrient content. Specifically, higher RQ was associated with lower bids for carbohydrate, but not fatty or combo foods. These findings demonstrate that fuel use influences the value of carbohydrates, revealing a novel association between nutrient partitioning and food reinforcement. Analyses are ongoing to investigate the neural correlates of this effect with fMRI.

3:00

Caloric Value Is Transferred To Anticipatory Cues As Interoceptive Predictions In Humans (George H.Collier New Investigator Travel Awardee)

Elayna Seago¹, Afroditi Papantoni¹, Jessica Liu^{1,2}, Kyle Burger¹

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

Cues in our environment that signal the presence of reinforcing foods become salient through conditioning, i.e., incentive sensitization. Little is known about the role of sugar and flavor and impact of weight status (BMI) on this process. We hypothesized that regions that encode reinforcement, salience, and gustatory interoception would show sensitization to cues over time and that this would be stronger in participants with higher BMI. Healthy adults (n=111; F=67; BMI=23.4 $\pm$ 3) were exposed to cues and tastes of flavor-matched sugar-sweetened (SSB) and unsweetened beverages (USB) during an associative learning fMRI paradigm. Main effects of SSB taste > USB taste were performed across the whole brain. To assess conditioning, parameter estimates (SSB cue > USB cue) were extracted from 4 regions of interest (ROI), the midinsula (MI), dorsal striatum, ventral striatum and ventral pallidum, and the precuneus, at 4 time points (4 events

per time point). Percent signal change was used in longitudinal multilevel models with tests for BMI moderation. In response to SSB taste (>USB taste), we observed bilateral amygdala activity extending into the ventral striatum (pFDR's<0.005; Z's > 4.3). We also observed an interaction between BMI and time (b=0.02; p=.012) where participants with a higher BMI showed greater cue sensitization in the MI. No significant effects were observed in the other ROIs. Greater change in MI response reflects amplified encoding of anticipated interoceptive signals of calories, particularly in individuals with elevated BMI. Alongside amygdala/ventral striatal response to SSB taste, this suggests that caloric value is encoded as an outcome and transferred to cues as interoceptive predictions, consistent with incentive sensitization beyond sensory features.

3:15 **Translating The Gliotransmitter Octadecaneuropeptide Into A Once-Weekly Injectable Therapeutic, Dg-260, For The Treatment Of Obesity And T2Dm Without Adverse Events (Randall R. Sakai New Investigator Travel Awardee)**

Keshav/S Subramanian¹, Oleksandra Orativskyi², Haley Maury², Drew Belser¹, Brandon Alonso¹, Ashley Lee¹, Chloe Do¹, Quindy Pan¹, Bart/C De Jonghe¹, Caroline/E Geisler³, Robert/P Doyle^{2,4}, Matthew/R Hayes¹

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Obesity and type 2 diabetes mellitus (T2DM) are among the most common diseases but still lack effective long-term curative treatments. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have shown astonishing effects in treating obesity and T2DM; however, they are associated with gastrointestinal adverse events, leading 2/3 of patients to discontinue their treatment within the first year and regain their lost body weight. Recent work from our lab showcased an octadecaneuropeptide (ODN) analog, tridecaneuropeptide (TDN), which acutely and chronically reduces bodyweight and improves glycemic control without nausea/emesis in rodents. Here, we present work on the development of a long-acting lipidated-TDN analog, DG-260, which potently reduces food intake and bodyweight in lean and diet-induced obese (DIO) mice upon acute systemic injection. In addition, using euglycemic clamps, DG-260 dramatically improves systemic insulin resistance in DIO mice through increased peripheral glucose clearance rates and insulin secretion. To evaluate the longitudinal impact of repeated DG-260 delivery, we measured daily high-fat diet (HFD) intake and bodyweight in DIO mice for 30 days receiving DG-260 injections every 48h in comparison to the GLP-1RA, semaglutide. DG-260 dose-dependently suppressed HFD intake and reduced bodyweight, culminating in reduced cumulative HFD intake and daily bodyweight loss comparable to the ~20% weight reduction of semaglutide. Furthermore, semaglutide-treated animals switched to DG-260 showed sustained bodyweight loss and HFD suppression. Lastly, dose escalation of DG-260 significantly increased the HFD intake and bodyweight reducing effects. Overall, these data show the enormous potential of DG-260 as an alternative, long-acting non-GLP-1 based therapeutic.

3:30 **Stress Engages The Noradrenergic Brainstem-Hypothalamus Loop That Suppresses Appetite Persistently (New Investigator Travel Awardee)**

Myungmo An, Junkoo Park, Sumin Lee, Se-Young Choi, Sung-Yon Kim
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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. Inhibition of LC^{NA} neurons or their projections to the paraventricular hypothalamus (PVH) prevents stress-induced appetite suppression, whereas optogenetic activation of LC^{NA} neurons mimics stress effects that suppress feeding. Real-time norepinephrine recordings in the PVH show sustained elevation after restraint stress, correlating with the duration of feeding suppression. Pharmacological blockade of α 1-adrenergic receptors abolishes stress-induced appetite suppression. Notably, this circuit is also required for feeding suppression after chronic stress. Our findings pinpoint the LC^{NA}-PVH ^{α 1} noradrenergic circuit as a key driver of sustained appetite suppression following stress, uncovering a direct link between the brainstem arousal center and hypothalamic feeding circuits.

3:45 **Single Nutrient Overconsumption Induces Nausea And Increases Gdf15 Levels In Rats, Effects Attenuated By Chronic Exposure To A Western Diet (New Investigator Travel Awardee)**

Allison M. Pataro^{1,2}, Sophia L. Fischer^{1,2}, Serena X. Gao^{1,3}, Ann Law¹, Fatma Cicek¹, Madeline Medina^{1,4}, Tito Borner¹

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Overconsumption of energy-dense foods plays a critical role in the development of obesity. Because of their high palatability, people may exceed the satiation threshold and overeat to the point of feeling nauseous, yet the relative contributions of volume versus nutrient composition to this response remain unclear. To begin disentangling these factors, we investigated how the overconsumption of a whole liquid meal or single macronutrient solutions affects satiation and malaise. Rats received gastric isocaloric and isovolumetric infusions of either a mixed-nutrient meal (Ensure), fat, sugar, or water. Subsequently, kaolin consumption (a proxy for nausea in non-vomiting rats), food intake, and plasma concentrations of GDF15, a cytokine known to promote nausea, vomiting, and anorexia, were measured. All gastric caloric infusions significantly reduced food intake, while water had no effect. Notably, isolated nutrient solutions induced kaolin intake and

significantly elevated plasma GDF15 levels, whereas Ensure did not, indicating that nutrient composition rather than caloric load or volume drives nausea. Pharmacological blockade of serotonin receptors with ondansetron failed to attenuate nausea, suggesting a mechanism independent of serotonergic signaling. Importantly, in rats maintained on a high-fat/high-sugar diet, nutrient-induced kaolin consumption and elevated GDF15 levels following caloric load are significantly blunted. This suggests that exposure to a Western diet reduces overconsumption-induced malaise through blunted GDF15 signaling. Together, these findings identify GDF15 as a candidate mediator of nutrient-specific malaise and reveal that chronic exposure to energy-dense diets dampens this signaling system, potentially facilitating continued overconsumption.

4:00

In A World Of Protein Shakes And Glp-1S: Sex Divergent Effects Of Semaglutide On Muscle Composition And Protein Intake In Rats (Dorothy W. Gietzen New Investigator Awardee)

Mya A. Knappenberger¹, Madison T. Bento², Morgan R. Sotzen², Suyeun Byun¹, Annalise M. Kuhns¹, Doris Olekanma¹, Karolina P. Skibicka²

¹The Pennsylvania State University, University Park, PA, United States, ²The University of Calgary, Calgary, AB, Canada

GLP-1-based anti-obesity therapies like semaglutide (SEMA) are widely used for weight loss, but their potential to reduce lean mass is intensely debated. How these treatments affect muscle function, composition and protein appetite and preference, and whether these effects differ by metabolic state or sex, remains unclear. We treated lean and diet-induced obese (DIO) rats with SEMA for 4 weeks and compared their muscle mass with ad libitum control and pair-fed (PF) rats (n=12/group). SEMA reduced gastrocnemius mass in lean and DIO males (-11%, -8% vs. controls, p<0.05), but not females, indicating an obesity-independent sex difference. In DIO rats, control males improved wire hanging over time, whereas SEMA-treated males did not, suggesting impaired muscle function. In contrast, SEMA-treated females improved muscle function, which correlated with lower body weight, suggesting that reduced body mass may partly underlie this effect. Given the relationship between protein intake and muscle function, we determined whether SEMA affects protein preference. Lean, but not DIO, SEMA-treated rats increased their protein preference in a sex-independent manner. Motivated behavior for protein consumption, assessed by PR operant test for high vs low protein, was not altered across groups. SEMA-treated DIO males also showed reduced protein preference in a macronutrient preference test (7.36 vs. 12.45 kcal, ~40% decrease, p<0.05), an effect not observed in females. These findings suggest that protein preference is differentially regulated by biological sex and metabolic state and suggest impaired protein prioritization in males, when competing nutrients are available. These findings reveal sex-specific and largely obesity independent effects of SEMA on muscle and protein appetite.

4:15

Npy And Opioids Inhibit Vagal Afferent Activation Of Nts-Npy Neurons (New Investigator Travel Awardee)

Josefina I Jara, Luciano Fernandes, Suzanne M Appleyard
Washington State University, Pullman, WA, United States

Activation of the majority of neuronal subpopulations in the nucleus of the solitary tract (NTS) suppresses food intake. In contrast, activation of neuropeptide Y neurons in the NTS (NTS-NPY) promotes food intake. Previous work from our lab showed these neurons receive direct excitatory vagal input and are activated by cholecystokinin (CCK). CCK is known to activate vagal afferents to inhibit food intake, yet our data suggest it may transiently drive NTS-NPY neuron activity early in a meal before being inhibited during satiation. However, factors that inhibit NTS-NPY neurons remain unclear. Here, we examined the effects of NPY and opioids, neuropeptides known to inhibit other NTS neurons. We performed voltage clamp recordings from brain slices containing the NTS and vagal afferents in the solitary tract (ST) from male and female mice. NPY neurons were identified by crossing NPY-Cre and loxP-tdTomato mice. We recorded evoked excitatory postsynaptic currents following ST stimulation (10 pulses, 50Hz, ST-EPSC). NPY (100nM) reduced the amplitude of ST-EPSCs by 31% (n=34, p=0.002) with greater inhibition in females (0.58±0.01-fold) than males (0.81±0.05-fold, p=0.03). To test whether nutritional state influenced this effect, we compared ad-libitum-fed and fasted animals. NPY reduced presynaptic release probability in fasted females, with an 80% increase in paired-pulse ratio (n=34, p=0.005). Similarly, the μ - and δ -opioid agonist metenkephalin (100nM) strongly inhibited ST-EPSCs by 90.5% (n=8, p=0.003). These findings indicate that NTS-NPY neurons are inhibited by NPY and opioids. As these neurons express NPY this could provide a potential feedback mechanism to suppress vagal activation of these pro-feeding neurons at later stages of a meal.

6:45 - 8:45 PM	Offsite
New Investigators Social	

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Saturday, August 8, 2026

9:00 - 10:00 AM

Regency A

Poster Session 4-1

P301

Consumer Visual Attention To Food Packaging Information: An Eye-Tracking Study Considering Health Status

Pablo Arrona Cardoza, Daiva E Nielsen

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Rationale: There is much interest in using food packaging information to promote healthy food choices. However, prior research has not considered whether consumer health status plays a role in visual attention to this information. Hypothesis: Compared to consumers without a chronic condition, consumers living with Type 2 Diabetes (CwT2D) will give greater visual attention to nutrition information on food packaging. Species: Human participants, aged 40-65 years. Number of subjects: Forty-three participants (19 CwT2D, 24 comparison group). Procedures: Participants completed a shopping task in a food retail setting while wearing eye-tracking glasses (Tobii Pro Glasses 3). Areas of interest (AOI) were defined for food packaging components: Brand, Product Image(s), Nutrition Facts Table (NFT), Ingredients List, Marketing Claims, Other Text, and Price Promotion. Total view time (TVT) was calculated for each AOI and linear mixed-effects models evaluated differences in TVT between study groups. A binary outcome (viewed vs. not viewed) was also computed for each participant and each AOI. The probability of an AOI being viewed was analyzed using logistic mixed-effects models. Results: There were no differences in TVT between study groups ($p=0.778$), but among both groups, NFT was viewed significantly longer than ingredients, marketing claims, and price promotion (all $p<.0001$). Among both groups, front-of-pack AOIs, such as brand (prob=.96) and label text (.94), were highly viewed, while back-of-pack AOIs, such as NFT (.60) and ingredients (.19), were viewed less frequently. Relevance: In this sample of consumers, contrary to our hypothesis, visual attention to food packaging information did not differ by health status. Among both study groups, while NFT were viewed longest when looked at, front-of-pack elements were more likely to be viewed.

P303

Nucleus Accumbens Dopamine Tracks Individual Differences In Operant Food-Seeking Engagement

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Mesolimbic dopamine signaling in the nucleus accumbens (NAc) is a key regulator of food motivation and reward-seeking behavior. Prior studies demonstrated that dopamine activity predicts task engagement and action initiation, but far less is known about how endogenous dopamine dynamics relate to individual variability in operant responding. Here, we tested whether differences in responding to various reinforcement schedules are associated with the extent of dopamine signaling during food seeking. We recorded NAc dopamine activity using fiber photometry with expression of the GRABDA sensor (pAAV-hSyn-GRAB-rDA3m) in male and female C57BL/6J mice. Mice were trained on a fixed ratio schedule in which a correct response was reinforced with a 20 mg sucrose pellet. After acquisition, NAc dopamine was recorded during task performance in a behavioral chamber. High-responding mice exhibited larger dopamine signals around correct response events compared to low responding mice, even when yoking analyses to the same number of trials. Additionally, dopamine peak activity was observed to shift in time between early and late trials, suggesting that dopamine dynamics change across task progression. Together, these findings indicate NAc dopamine dynamics are proportionally linked to overall responding across a motivational task, vary with individual mouse performance, and are shaped by ongoing task experience.

P305

Examining Early Dietary Influences On Toddlers' Food Acceptance: Evidence From The Mint Study

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Early feeding experiences may shape food acceptance, but evidence remains limited. Building on the MINT randomized controlled trial, which examined protein-rich complementary diets and infant growth, this study evaluated whether early exposure to protein-rich foods was associated with toddlers' acceptance of these foods. Infants (N=115) were randomized to consume dairy, meat, plant-based protein foods, or an ad libitum diet from 5–12 months. Between 18–24 months, caregivers reported toddlers' exposure to and liking of protein-rich foods. A behavioral session followed, in which children's acceptance of and preference for cheddar cheese, turkey, and black beans were assessed. Preliminary analyses involved a series of 4 (Group) x 3 (Food) repeated measures analyses. Caregivers (N=115) were predominantly mothers (90%) and White (66%), and toddlers (54% female) were 20 months old (SE=0.2), with 73% breastfed for at least 6 months. At the time of the survey, caregivers reported that children consumed dairy most frequently, followed by meat and then plant-based protein foods, except

in the dairy group, which consumed dairy less frequently than the other groups ($p < 0.001$). In contrast, caregivers reported greater liking of dairy compared to other foods among children in the dairy and ad libitum groups, whereas no such differences were observed in the meat or plant-based groups ($p < 0.001$). During the behavioral sessions, the intake of cheese was significantly higher than that of the other foods ($p < 0.001$) for all groups. However, intake of the test foods did not differ as a function of early exposure. Overall, these preliminary findings suggest that early exposure to protein-rich foods may not be associated with differential acceptance of these foods during toddlerhood.

P307

Satiety And Food Liking Drive Meal Cessation In Minimally And Ultra-Processed Breakfast Meals

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Excess intake driven by hyperpalatable food and delayed satiety is a proposed mechanism linking ultra-processed food (UPF) and obesity. This study examines Reasons Individuals Stop Eating Questionnaire (RISEQ15) scores in meals differing in UPF and nutritional quality (NQ). A crossover trial had 3 visits. At visit 1 demographic and anthropometric measures were taken. At all visits subjects ate 1 of 3 meals of like foods matched for energy and macronutrients in random order: non-UPF high NQ (NUPF-HNQ), UPF high NQ (UPF-HNQ), and UPF low NQ (UPF-LNQ). Subjects ate alone at their own pace to comfortable satiety. A state RISEQ15 was given and appetite and palatability assessed by visual analog scale after meals. A composite hedonic score (CHS) averaged pleasant, tasty, and texture ratings. RISEQ15 includes 3 questions in each of 5 domains: decreased food appeal (DFA), physical satisfaction (PS), planned amount (PA), self-consciousness (SC), and decreased priority of eating (DPE). Higher scores suggest stronger meal cessation drivers. Repeated measures analysis of variance tested between meal differences in RISEQ15 scores at $p < 0.05$. Lower scores are expected for UPF-LNQ than UPF-HNQ and NUPF-HNQ. 30 adults mean age 25.9 ± 4.9 y and BMI 25.0 ± 4.4 kg/m² (65% white, 67% female) completed RISEQ15 at > 2 visits. PS scores were highest and satiety ratings high (49.9 - 71.7 mm) at all meals. For NUPF-HNQ and UPF-HNQ scores in order were PA, DFA, DPE, SC. For UPF-LNQ scores in order were DFA, PA, DPE, SC. DFA was higher ($p = 0.02$) and CHS lower ($p < 0.05$) for UPF-LNQ than NUPF-HNQ and UPF-HNQ with a weak negative correlation for CHS and DFA ($r = -0.36$, $p < 0.01$) and no correlation for PS and satiety. PS primarily drove meal cessation, while DFA correlated with CHS and palatability ratings.

P309

Early-Life Food Insecurity Impacts Body Weight Later In Life In Female Rats.

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Early-life food insecurity has been linked to adverse cognitive and metabolic outcomes, but causal connections remain speculative. Here we tested the hypothesis that exposing female rats to our early-life food insecurity model would produce long-term behavioral impairments and alter responses to an obesogenic diet in adulthood. Female Sprague Dawley rats were randomly divided into 3 groups ($n = 9$ - 10 /group): Secure-Chow (SC), Secure-Mixed (SM), or Insecure-Mixed (IM). Using programmable feeders, food access was manipulated by timing, type, and quantity during development from postnatal days (PNs) 26-45. From PN46 onwards, all rats received chow ad libitum until the cafeteria diet challenge (CAF; 11% sucrose solution + 60% from fat diet) from PN170-220. In adulthood (PN60+), rats were assessed in zero maze, open field, delay discounting, novel object recognition, novel location recognition (NLR), novel object in context, and a novel meal location paradigm. In contrast to our published findings in males, IM female rats showed no group differences relative to controls on any behavioral measures, including hippocampal-dependent memory. During subsequent CAF diet exposure from PN170-220, there were no group differences in kcal intake, yet the IM group's body weights were significantly greater than the SC group's body weights by the end of the CAF diet challenge ($p < 0.05$), an effect not observed in males exposed to a similar CAF diet. These findings suggest that the long-term consequences of early-life food insecurity are sex-dependent, with females potentially being more sensitive to weight gain when challenged with CAF diet.

P311

Beyond Liking: Mapping Behavioral Drivers Of Snack Intake From Natural Consumer Language

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Consumer research on snack foods often focuses on liking and preference, yet these measures alone may not predict real-world intake behavior or repeated consumption. We hypothesized natural consumer language in online reviews reveal behavioral drivers of snack choice beyond hedonic preference, including reward reinforcement, contextual consumption, and self-regulation processes. Over 3,000 Amazon "Chips & Crisps" reviews were analyzed using a machine-learning semantic topic discovery approach designed to preserve experiential meaning rather than isolated keywords. Consumer language clusters were interpreted through an LLM-assisted behavioral framework integrating COM-B constructs, habit formation theory, reward reinforcement, and contextual consumption mapping. Sensory characteristics such as crunch, salt intensity, greasiness, and freshness frequently functioned as behavioral gatekeepers influencing repeat consumption and product abandonment rather than simple liking alone. Reviews of "healthier" chip products frequently reflected negotiation between indulgence and self-regulation, with consumers valuing reduced guilt while maintaining reward value. Habitual and social intake contexts (movie nights, travel, family routines) repeatedly emerged as reinforcement structures associated with repeated consumption independent of stated preference. Consumers also expressed conflicting goals simultaneously (e.g., indulgent yet healthy, crunchy yet light), suggesting snack choice may involve resolving behavioral tensions rather than optimizing single sensory attributes. These findings suggest online consumer language may provide an ecologically valid source of ingestive behavior data extending beyond traditional preference measurement.

P313

It Doesn't Feel Like Charity; It Feels Like A Privilege (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))

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Due to persistent food insecurity, many households rely on food support, predominantly food banks, to access sufficient food. However, food banks and other charitable responses to food insecurity often fail to meet people's nutritional demands in a socially acceptable and dignified way. The potential of social enterprises to provide alternative forms of food provision has been suggested but is under-explored. The current research qualitatively explored recipients' experiences of two food projects (Slow Cooker and Meal Box projects) provided by a UK-based social enterprise, Can Cook, in collaboration with social housing provider, Riverside, within urban areas of socioeconomic disadvantage. Telephone interviews explored recipients' pre-project access to food and their experiences of taking part (n=25; 96% women; 92% in food insecurity; 100% living in social housing). Thematic analysis revealed four overarching themes: (1) Pre-project food access experiences; (2) Experiences of the food project(s); (3) Benefits of participation; (4) Barriers to engagement. Participants' pre-existing food insecurity was a major contributor to their mental and physical ill-health. Accessing the Can Cook project(s) enabled perceived improvements to food insecurity symptoms, food skills, confidence, health and psychological wellbeing. However, these benefits disappeared upon project completion, with participants defaulting back into food insecurity. These findings provide case-specific evidence of the potential for social enterprise models to act as an innovative alternative to food banks to address the seemingly intractable issue of food insecurity in the UK. However, longer-term support and upstream changes are needed to enable sustained improvements to food insecurity to be achieved.

P315

Dopamine D2 Modulation Decreases Striatal Response To Gustatory Reward And Energy-Dense Food Intake Humans

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Given flexibility and rigor in animal models, dopamine's role in reinforcement signaling is well characterized preclinically, but less experimental research is available in humans. We conducted an fMRI trial to test the effect of Bromocriptine, a dopamine D2 agonist, on gustatory reward during fMRI, ad libitum intake of energy-dense foods, and explicit preference valuation. We hypothesized that dopamine agonism would increase BOLD response in the ventral striatum (VS) during milkshake receipt, decrease food intake, and have no effect on preference ratings. Adults (n=38; BMI=29.1±3.6) received Bromocriptine (1.6mg) and placebo on separate, counterbalanced days. In each session, participants completed an fMRI paradigm that paired cues with a milkshake or a tasteless solution (TS), with milkshake > TS indexing reward. VS region-of-interest analyses (P_{fwe}<0.05) were conducted. Under the placebo condition, we observed a significant VS response to the milkshake reward (P_{fwe}<0.01; k=6, T=4.1). However, Bromocriptine (vs. placebo) attenuated this response (VS; P_{fwe}=0.20). Bromocriptine also decreased energy-dense food intake (mean difference = -74 kcal; p=0.03), without impacting average ratings of liking (p=0.68) or wanting (p=0.35) of the foods. Results indicate that D2-mediated modulation attenuates striatal gustatory reward response and energy intake outside of explicit valuation. These effects and the relatively small dose of Bromocriptine suggest a possible mechanism whereby the dopamine D2 agonist acted presynaptically on autoreceptors, resulting in lower tonic and likely phasic dopamine response to reinforcing stimuli. A preclinical model evaluating Bromocriptine versus control using GRAB-DA would directly test this hypothesis.

P317

Effect Of Forced-Choice Format On Gustatory Performance And Response Validity In The Waterless Empirical Taste Test (Wett)

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Rationale/Premise: The Waterless Empirical Taste Test (WETT) includes a “no taste” option that may be strategically overused, reflecting response behavior rather than true sensory function. Hypothesis: Removing the “no taste” option will alter response patterns but not underlying gustatory performance when scoring is harmonized. Species: Humans Number of Subjects: 98 healthy participants (75 women; age 6–76 years) Procedures: Participants completed two within-subject WETT administrations: (1) standard 6-alternative format (including “no taste”) and (2) forced 5-alternative format without it. Total and taste-specific scores were compared using paired t-tests. Standard scores were adjusted by removing “no taste” responses to enable direct comparison with forced-choice performance. Results: Total scores were higher in the standard format (34.0 ± 8.9) than in the forced-choice format (25.1 ± 9.0; t(97)=10.08, p<0.001), driven by frequent “no taste” selections. Critically, adjusted standard scores (24.1 ± 7.7) did not differ from forced-choice scores (p=0.20), indicating stable underlying performance. Taste-specific responses were consistent across formats, with only a modest increase in sweet selections under forced choice (p=0.029). Conclusions/Relevance: Response format influences reporting behavior without altering underlying gustatory function. These findings suggest that discrepancies between standard and forced-choice formats may serve as a behavioral marker of non-credible responding. This paradigm provides a practical framework for assessing response validity in ingestive behavior research and clinical taste testing.

Hippocampus Dopamine Meal Responses Require Nutrients And Modulate Episodic Meal Related Memory And Satiety Via D2R Receptors

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Dopamine (DA) is a neurotransmitter critically involved in food-related reinforcement learning. DA function in the hippocampus (HPC), a brain region known for its role in episodic memory and food intake control, is poorly understood. Here, we investigated dorsal HPC DA binding during meal consumption using *in vivo* fiber photometry recordings with DA receptor-based fluorescent sensors in rats. We found increases in DA binding when comparing the pre-meal to the post-meal state in fasted rats fed either a standard chow, a high fat high sugar diet, or a liquid sucrose solution. However, neither consumption of a sweet-tasting non-caloric saccharine solution, nor intraperitoneal injections of either glucose or the satiation hormone cholecystokinin, influenced DA binding in the HPC. These results indicate that pre- to post-meal HPC DA increases require caloric intake. To assess the function of post-meal HPC DA signaling, we evaluated the effects of neuropharmacological manipulation of HPC DA 2 receptors (D2Rs) on eating and food-based mnemonic behaviors. Results revealed that HPC-targeted D2R activation reduced cumulative food intake via reductions in meal size. While HPC D2R antagonism did not influence cumulative food intake, it reduced the latency to initiate eating following a salient meal consumed outside of the home cage, as well as memory for the location of a recent salient meal. We interpret these collective results to suggest that HPC DA-D2R signaling is a candidate neurochemical mechanism through which nutrient consumption promotes meal-related episodic memory and satiety.

P321

Soluble Human Amyloid Beta In The Hypothalamus May Potentiate Peripheral Metabolic Impairments In TgF344-Ad Rats In A Sex-Dependent Manner

Cameron Caggiano¹, Caleb M Levine¹, Thea Anderson¹, Michael A Kelberman², David Weinshenker², Hannah L Lail¹, Desiree Wanders¹, Debra A Bangasser¹, Scott E Kanoski³, Marise B Parent¹

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Previous evidence suggested that TgF344-AD rats may be prone to weight gain during early Alzheimer's disease (AD) development, leading us to hypothesize that soluble brain amyloid impairs peripheral metabolism. To test this, energy intake, body mass and composition, and the impact of a high fat/high sugar diet (HFHS) and glucose administration on blood glucose were assessed in male and female TgF344-AD rats and their wildtype (WT) littermates (N = 65). Body temperature, interscapular brown adipose tissue (iBAT) mass, and western blot iBAT uncoupling protein-1 (UCP1) expression were used as indicators of thermogenic function. Soluble amyloid A β 42 (A β 42) was quantified in hypothalamus using ELISA. Data were analyzed with mixed linear models and Bonferroni-corrected pairwise t-test post-hoc tests. The results showed sex differences in energy homeostasis that correlate with hypothalamic A β 42. Specifically, male TgF344-AD rats began to outweigh WT rats by 5 weeks of age; this increase emerged at ~ 5 months in female TgF344-AD rats. Female TgF344-AD rats ingested more energy from chow and the HFHS diet, gained more weight on the HFHS diet, and had lower UCP1 than WT rats, effects not observed in male TgF344-AD rats. Male and female TgF344-AD rats had increased body temperatures, which was restricted to the dark phase in females — when they ingested excess calories. The HFHS diet disrupted glucose regulation in only male TgF344-AD rats. Hypothalamic A β 42 correlated with glucose dysregulation in male TgF344-AD rats and BAT mass in female TgF344-AD rats, raising the possibility that increases in hypothalamic A β 42 produce sex-specific disruptions in energy homeostasis and that peripheral metabolic changes may be an early symptom of AD development.

P323

Sex Differences In Macronutrient Preference And Dopamine Signaling Following Post-Ingestive Nutrient Sensing

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Dietary choice plays a critical role in metabolic and neurological health, yet the biological factors that shape macronutrient preference remain poorly understood. Evidence from both humans and rodents suggests potential sex differences in the attractiveness of specific nutrients, though findings have been inconsistent. Recent work indicates that post-ingestive gut-derived signals can modulate midbrain dopamine (DA) systems to influence food reward. Here, we examined the possibility that sex differences in macronutrient preference may arise from differential engagement of these pathways. In experiment 1, adult male (n = 12) and female (n = 11) C57BL/6J mice were given simultaneous access to fat, sucrose, or a fat-carbohydrate combination across 14 days. Intake and behavioral measures were quantified and estrous cycle stage was monitored in females. Females showed a selective increase in fat intake relative to males, which preferentially consumed the combination food. Estrous cycle stage was associated with increased intake and greater consumption of the combination food stimulus. In experiment 2, we measured midbrain activation following intragastric nutrient infusions (n=18 males/females). This data revealed sex-specific activation patterns in the substantia nigra pars compacta, but not the ventral tegmental area, particularly in response to fat-containing nutrients. In experiment 3, we measured terminal DA release in both the dorsal striatum (N=6) and nucleus accumbens (N=8), and discovered sex specific patterns of DA responses to macronutrients that corresponded with post-ingestive effects on midbrain neurons. Together, these findings demonstrate robust sex differences in macronutrient preference that may reflect differences in post-ingestive modulation.

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Optogenetic Activation Of Npy Terminals Suppresses Vagal Afferent Transmission In The Nucleus Tractus Solitarius

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Visceral sensory signals from the gastrointestinal tract are conveyed via vagal afferents to the nucleus tractus solitarius (NTS), where neurons relay this information to regions that control food intake. NPY-containing projections innervate the NTS, and NPY microinjection into the NTS increases food intake, but their role in shaping neuronal excitability and vagal activation remains unclear. We performed patch-clamp recordings from NTS neurons in brainstem slices from NPY-Cre mice expressing channelrhodopsin-2 (NPY-Cre x Ai32 ChR2) while electrically stimulating the solitary tract (ST). Optogenetic activation (30 Hz, 15 s) of NPY terminals robustly suppressed spontaneous action potential firing of unlabeled NTS neurons from 4.15 ± 3.21 to 2.28 ± 3.09 Hz (0.55-fold of control; $n=14$). This effect was not blocked by GABA_A receptor antagonism (picrotoxin, 0.29 ± 0.09), GABA_B receptor antagonism (picrotoxin+CGP35348, 0.64 ± 0.14 - or Y2 receptor antagonism (picrotoxin+BIIE0246, 0.12 ± 0.10). In contrast, combined blockade of GABA_A, Y2, and $\alpha 2$ -adrenergic receptors (picrotoxin+SKF97541+BIIE0246) significantly attenuated the effect (1.076 ± 0.20 -fold of control; $n=8$). Optogenetic activation also reduced vagal input, as the amplitude of ST-evoked excitatory postsynaptic currents (eEPSCs) decreased (0.74 ± 0.06 of control; $n=5$; $p=0.0391$). These findings indicate that activation of NPY terminals suppresses neuronal excitability and vagal afferent signaling in the NTS. They also suggests that co-release of NPY and norepinephrine is required, providing a mechanism by which these neurons can inhibit NTS neuronal activity and gate vagal input to regulate ingestive behavior.

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Endogenous Glp-1R Signaling Encodes Responses To Rewarding And Aversive Food StimuliChloe X. Guo¹, Gulsun Memi^{1,2}, Taha B. Gungul¹, Ali D. Guler¹¹Department of Biology, University of Virginia, Charlottesville, VA, United States, ²Department of Physiology, School of Medicine, Adiyaman University, Adiyaman, Turkey

Glucagon-like peptide-1 receptor agonists (GLP-1RAs), such as semaglutide (Ozempic/Wegovy), have generated substantial public and scientific interest because of their successful weight loss effects. These compounds are modified from the endogenous GLP-1 hormone and act through glucagon-like peptide-1 receptors (GLP-1Rs). However, how endogenous GLP-1R signaling regulates energy balance in the brain remains unclear. Here, we show that GLP-1R neurons encode the transition from foraging to consumption, with region-specific populations differentially regulating responses to rewarding and aversive food stimuli. To systematically evaluate this, we examined five GLP-1R-expressing brain regions: paraventricular hypothalamus (PVH, $n = 7$), dorsomedial hypothalamus (DMH, $n = 7$), dorsal lateral septum (dLS, $n = 11$), ventral tegmental area (VTA, $n = 10$), and central amygdala (CeA, $n = 10$). In all regions except the CeA, GLP-1R activity consistently decreased in response to rewarding foods and increased in response to aversive stimuli. In contrast, CeA GLP-1R neurons displayed increased activity to select rewarding foods across pre-ingestive, ingestive, and post-ingestive phases. Our findings position the CeA as a key integrator of food reward value across feeding phases, with implications for improving GLP-1 therapeutics.

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Repeated Chemogenetic Excitation Of Vagal Afferents Expressing Oxytocin Receptors Promotes Negative Energy Balance In Obese MiceDominique N. Johnson^{1,2}, Jeremiah Isaac^{1,2}, Guillaume de Lartigue³, Karen A. Scott^{1,2}, Annette D. de Kloet^{1,2}, Eric G. Krause^{1,2}¹Neuroscience Institute, Atlanta, GA, United States, ²Center for Neuroinflammation and Cardiometabolic Diseases, Atlanta, GA, United States, ³Monell Chemical Senses, Philadelphia, PA, United States

Obesity is a chronic disease partly driven by disrupted interoception, the process by which an organism senses and interprets bodily signals. In obesity, gastrointestinal mechanosensation, which typically limits food intake, is blunted. Vagal afferents, whose soma are in the nodose ganglion (NG), are key mediators of this process, and this includes a discrete population of mechanosensing neurons that express oxytocin receptors (NG^{Oxtr}). Chronic chemogenetic activation of these NG^{Oxtr} leads to decreased food intake and body weight in lean mice, but it is unclear whether these neurons remain targetable in obesity. To address this, Oxtr-Cre mice received NG injections of Cre-inducible AAVs to direct designer receptors exclusively activated by designer drugs (DREADDs)-Gq or control mCherry to NG^{Oxtr}. Mice were then given either 60% high fat diet (HFD) or remained on standard chow generating four groups (CON-HFD, CON- standard, Gq-HFD, and Gq- standard). After HFD-induced obesity was achieved, all mice were housed in a TSE Phenomaster to monitor food intake and energy expenditure and allowed to habituate to the testing procedures. Mice then received daily injections of clozapine-N-Oxide (CNO) for 12 days. Activation of NG^{Oxtr} reduced body weight and food intake in lean and obese Gq mice relative to controls. Reductions in energy expenditure further support the interpretation that body weight loss is the result of hypophagia, rather than increased activity. In addition, there was no compensatory feeding, leading to maintained weight loss for weeks after treatment stopped. Overall, these studies demonstrate that NG^{Oxtr} remain responsive in obesity and represent a target for restoring satiety signaling and achieving weight loss.

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A Loss Of Palatable Reward Processing In An Alzheimer'S Disease Rat ModelBrianna E Linneman^{1,2}, Leighelle A Adrian¹, Mark Niedringhaus^{1,2}, Elizabeth A West^{1,2}¹Department of Neuroscience, Rowan-Virtua School of Osteopathic Medicine, Stratford, NJ, United States, ²Rowan University School of Translational Biomedical Engineering and Sciences, Stratford, NJ, United States

Alzheimer's disease (AD) is characterized by neuropathological markers and cognitive decline, however, noncognitive AD symptoms, like apathy, are often overlooked. Using a transgenic AD rat model that shows age-dependent cognitive deficits and histological markers (TgF344-AD; AD rats), we investigated motivated behavior linked to ventral tegmental area (VTA) to nucleus accumbens (NAc) dysfunction. We utilized a conditioned place preference (CPP) assay in which one chamber was paired with a palatable food reward, and the other was paired with food chow (6 pairings each, 1 pairing/day) in AD and wild-type (WT) littermate controls at ages 2-3 and 6-7 months (n=11-13/group). 2-3-month-old WT and AD rats formed a preference to the reward paired chamber, while 6-7-month-old AD rats showed no preference. We also found a decrease in reward consumption in AD rats at 6-7-months but not at 2-3-months, suggesting age-related deficits in the motivational value of the reward. To investigate whether learning deficits contributed to the lack of CPP in 6-7 month old AD rats, we evaluated associative learning in a Pavlovian conditioning task. Rats underwent surgery for infusion of GRABDA and implantation of an optical ferrule into the NAc core. Rats underwent 10 days of conditioning, where they were presented with one cue that predicted a palatable reward (CS+) and a different cue that did not (CS-), while dopamine transients in the NAc were recorded using fiber photometry. Both WT and AD 6-7-month-old rats learn to distinguish between the cues by day 10. However, AD rats show altered dopamine dynamics during reward-predictive cues, but not during the reward itself. Thus, prior to the development of learning and memory issues, AD rats display altered motivation to palatable food rewards.

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Sex-Specific Recruitment Of Basolateral Amygdala Subpopulations Reflects Divergent Effects Of Stress On MotivationMegan McGraw, Emma Rose, Ai-Jun Li, Emily Qualls-Creekmore
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Stress can bidirectionally modulate motivated behavior as a function of its characteristics and context, a phenomenon implicated in substance use, eating disorders, and mood disorders, yet the underlying neural mechanisms remain unclear. Using a sex-inclusive model of social stress (chronic non-discriminatory social defeat stress; CNSDS), we reveal a striking divergence in appetitive operant responding, with responses enhanced in males and suppressed in females, and test the role of the basolateral amygdala (BLA) in driving these effects. Given its established role in integrating emotional valence with goal-directed behavior, the BLA is a strong candidate for mediating stress-induced changes in motivation. Despite similar overall activation of glutamatergic BLA neurons in response to CNSDS across sexes, this bulk signal obscures functionally distinct subpopulations. Prior work shows that Ppp1r1b+ neurons promote appetitive responding, whereas Rspo2+ neurons suppress it, indicating that their recruitment can oppositely regulate motivation. We hypothesize that CNSDS engages these subpopulations in a sex-specific manner aligned with behavioral outcomes. To test this, C57BL/6J mice underwent CNSDS for 2 or 10 days and were assessed for acute (cFos) and chronic (FosB) neural activation in the BLA, along with molecular identity (Rspo2/Ppp1r1b colocalization). We find sex-biased spatial activation, with females showing greater anterior BLA activity and males greater posterior activation, mirroring the distribution of aversive (Rspo2+) and

appetitive (Ppp1r1b+) neurons. Together, these findings identify a spatially and molecularly defined BLA mechanism that may underlie sex-specific vulnerability to stress-driven changes in motivated behavior.

P335 Effects Of Adolescent Semaglutide On Body Composition And Amygdala Function In Female Rats.

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Glucagon-like peptide receptor agonists (GLP-1RAs), including semaglutide (Sem), are approved for adolescent obesity due to weight loss effects, but impacts on body composition remain unclear. Adolescence is a critical period for amygdala development; in adults, Sem activates the central amygdala (CeA), involved in fear memory. Thus, drugs engaging this circuitry during adolescence may have lasting neural/behavioral consequences. Additionally, high fat high sugar (HFHS) obesogenic diets impact adolescent fear memory, and GLP-1RAs may mitigate these effects. We hypothesized that Sem would activate the CeA, influence amygdala-dependent memory, and attenuate HFHS-induced deficits. 48 adolescent female Sprague Dawley rats were assigned to four groups: control (CTL) with vehicle injections (Veh), HFHS with Veh, HFHS with Sem injections (SEM; 70 μ g/kg BW), and HFHS with Veh pair-fed (PF) to match caloric consumption of SEM. Body composition was assessed by DEXA. Amygdala-dependent fear memory was evaluated using auditory cued-fear conditioning. HFHS increased body weight and food intake versus CTL; SEM reduced both, with similar reductions in PF. SEM decreased fat accumulation ($p < 0.01$) and preserved lean mass versus HFHS, while PF did not reduce fat gain. HFHS impaired fear conditioning, with no significant difference in freezing to tone versus baseline. In contrast, SEM and PF showed intact fear memory ($p < 0.01$). These findings indicate Sem is more effective than caloric restriction alone in reducing adiposity in adolescent female rats. Behavioral results suggest HFHS impairs amygdala-dependent memory, which can be mitigated by reduced caloric intake. Further research is needed to determine the mechanism by which Sem and caloric restriction attenuate HFHS behavioral effects.

P337 Activation Of Prefrontal Cortex Subregions Differentially Alters Palatable Food Consumption In Obesity-Prone Rats: Implications For Translational Human Studies

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Weight gain occurs by positive energy balance, in which more calories are consumed than expended. Limited human studies suggest that a protein preload can reduce subsequent food intake in some individuals, and that activation of the lateral (l) prefrontal cortex (PFC) is correlated with inhibition of food intake, whereas activation of the medial PFC (mPFC) is correlated with its promotion. These findings can be tested for causality through rodent models using the rat functional analog of the IPFC, the prelimbic/infralimbic cortex (Pr/IL) and of the mPFC, the medial orbitofrontal cortex (mOFC). We tested normal-weight adult male and female Sprague-Dawley rats either predisposed to obesity (diet-induced obesity, DIO $n=36$) or obesity resistant (diet-resistant, DR $n=34$), and injected them with either a control (pAAV-hSyn-mCherry, $n=35$) or excitatory DREADD virus (pAAV-hSyn-hM3D(Gq)-mCherry, $n=35$) in either the Pr/IL or mOFC. After four weeks (for transfection), rats were given a protein or control preload (Ensure or water, within-subject) and then, after injection with a DREADD actuator or vehicle (CNO 3 mg/kg or saline IP, within-subject), were given access to palatable, sweet-fat pellets. Consistent with human studies, we found that (1) the protein preload reduced subsequent food intake in some individuals, but this did not depend on sex or DIO/DR status, (2) activation of the Pr/IL reduced food consumption in DIO rats after the protein preload, and (3) activation of the mOFC stimulated food consumption in DIO rats after the protein preload. Our findings suggest that activation of PFC subregions causally and differentially influences food intake in ways that may be influenced by genetic predisposition to obesity, providing insight into mechanisms underlying weight gain.

P339 Nmur2A-Based Poly-Agonists To Match High Efficacy With Unmatched Tolerability

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Neuromedin U receptor 2 (NMUR2) signaling modulates appetite control, positioning the receptor as an attractive therapeutic target for obesity. Activation of NMUR2 in hypothalamic circuits enables a differentiated approach to weight loss, and development of long-acting peptide agonists opens the door to potent and well-tolerated poly-agonists. Building upon our proprietary NMUR2 agonists, we explored combinations with complementary MoAs to enhance efficacy while retaining superior GI tolerability. Initial studies demonstrated additive efficacy of NMUR2 and GIPR agonism, producing dose-dependent, fat-selective weight loss. PoC in DIO mice led us to generate potent dual-agonists through targeted sequence engineering and lipidation, meeting our ambition for once-monthly administration in human. To systematically interrogate combinatorial mechanisms, we developed a multimodal neurophysiology platform integrating calcium imaging and electrophysiology in hypothalamic slices. This approach revealed distinct neuronal signatures and identified neurotensin receptor 1 (NTSR1) agonism as a synergistic match to NMUR2, yielding amplified network activation. Combination of a long-acting NMUR2 and NTSR1 agonists demonstrated synergistic food intake reduction and sustained weight loss in DIO mice. Notably, NTSR1 agonists did not enhance semaglutide's efficacy. Expression profiling

and behavioral assessment of NMUR2, GIPR, and NTSR1 agonists indicated minimal-to-no nausea or emetic risk. Collectively, these data position NMUR2-based poly-agonists as next-generation therapeutics combining high efficacy, improved tolerability without dose escalation, and provide a rational basis for synergistic peptide combinations compatible with convenient, infrequent drug administrations.

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Mapping And Characterization Of Discrete Medullary Innervation To The Ventral Tegmental Area (Vta).

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Ascending brainstem pathways relay interoceptive sensory information to various midbrain nuclei including the ventral tegmental area (VTA). The VTA then integrates this information to inform reward, appetitive, and emotional responses via dopaminergic projections to mesolimbic and mesocortical nuclei. Brainstem innervation of the VTA is sparse and largely contained in the nucleus of the solitary tract (NTS) and a small subpopulation of neurons in the ventrolateral medulla (VLM). Recently we mapped and characterized NTS to VTA-projecting neurons, however this analysis has not been applied to the VTA-projecting VLM neurons. Using VTA-targeted Retrobead injections, we found that a subpopulation of VLM neurons form monosynaptic connections with the VTA and were distributed throughout the rostro-caudal extent of the VLM. Immunohistochemical analysis showed that most VTA-projecting VLM neurons contained tyrosine hydroxylase (TH) and neuropeptide Y (NPY), with labeled neurons found throughout the VLM catecholamine groups (A1, A1/C1, and C1). Given the documented role of the VLM in glucose monitoring and regulation, we tested whether VTA-projecting VLM neurons were sensitive to glucoprivation. We measured c-Fos expression following fasting or fasting plus IP 2-deoxy-D-glucose (2DG) treatment and found ~35% of VTA-projecting VLM neurons were activated by glucoprivation, whereas very few (~10%) of the VTA-projecting NTS neurons contained 2DG induced c-Fos. We conclude that discrete populations of medullary catecholaminergic neurons provide the majority of ascending innervation to the VTA but show key differences in their responsiveness to glucoprivic challenge. The ability of these neurons to shape VTA output and appetitive behaviors remains to be determined.

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Single-Cell Profiling Of Sympathetic Control Of Ghrelin Secretion

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Ghrelin (GHRL) drives food intake during energy deficit, yet the sympathetic circuitry controlling fasting-induced GHRL secretion is unclear. We hypothesized that fasting induces cell-type-specific transcriptional remodeling in both the celiac ganglion (CG), which sends sympathetic input to the stomach, and gastric GHRL cells to regulate secretion. snRNA-seq of mouse CG (n=3) and bulk RNA-seq of FACS-isolated GHRL cells and whole stomach (n=2-4) were performed under fasting and re-fed conditions. Differential expressions were analyzed using MAST and GO enrichment. Integration of datasets generated a Projected Communication Score [presynaptic ligand expression $\times$ postsynaptic receptor fold change (FC)]. Synaptic Priming Score was calculated based on mean expression of synaptic GO modules. To define GHRL cell-specific fasting responses, the whole stomach calorie-restricted signature was subtracted from the GHRL cell transcriptome. Analysis of 8317 CG nuclei identified 3 sympathetic subtypes: SN1 (Npy+:27.8%), SN2 (Nrg1+:38.6%), and SN3 (Cntn5+:33.5%). SN1 neurons showed higher communication scores for NE $\rightarrow$ Adra1a and Npy $\rightarrow$ Npy5r interactions with GHRL cells vs. SN2/3 (p<0.0001). Fasting upregulated synaptic-like programs in GHRL cells, increasing the Synaptic Priming Score (mean diff=0.16, p=0.078, Cohen's d=3.54). Subtraction analysis showed 73.3% of the fasting response was GHRL cell-specific, including induction of synaptic-like programs and members of ERK1/2 signaling (p<0.05) such as *Cplx1* (FC=4.9), *Chrm3* (FC=2.7), *Fgfr2* (FC=2.4), and *Rras* (FC=1.7). These results identify a sympathetic axis that potentially primes GHRL cells for high-output secretion, revealing a coordinated CG-gut adaptation to energy deficit.

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A Gut-Olfactory Circuit Integrates Post-Ingestive Nutrient Signals To Support Odor Learning

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Food cues strongly influence eating behavior, yet how sensory cues become associated with the nutritional consequence of consumption remains unclear. The piriform cortex (PCx) encodes odor identity, undergoes associative plasticity, and mediates learned odor-guided behaviors. Whether post-ingestive nutrients reinforce odor representations through defined cortical circuits is unknown. We hypothesized that nutrient-responsive PCx neurons support odor-nutrient associations that guide eating behavior. **Results:** Using activity-dependent genetic labeling, we found that intragastric fat and sugar recruit a discrete ensemble of neurons compared to saline. In vivo miniscope calcium imaging further revealed rapid and prolonged PCx activation following nutrient infusions compared to saline, consistent with neural transmission of post-ingestive nutrient signals to the olfactory cortex. To determine whether these neurons contribute to odor-nutrient learning, we developed a novel odor-nutrient conditioning paradigm in which neutral odors were paired with the reinforcing post-ingestive effects of intragastric nutrients (Ensure). Preliminary results suggest that control mice form odor-nutrient associations, whereas caspase-mediated ablation of nutrient-responsive PCx cells impairs learning. **Conclusion:** These data suggest that post-ingestive nutrients reinforce odor cues, and that nutrient-responsive PCx neurons are necessary

mediators of odor-nutrient learning. This work identifies a novel gut-olfactory pathway through which internal nutritional signals may shape sensory representations to guide future food choice.

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An Amygdalopontine Pathway Promotes Motor Programs Of Ingestion

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Overconsumption of energy-dense, palatable food leads to obesity. We investigated neural circuit mechanisms that allow for the overconsumption of food despite visceral cues that signal fullness. We examined an inhibitory projection from the central amygdala (CeA) to the pons that targets the parabrachial nucleus (PBN), a well-established meal termination center, as well as the nearby premotor circuits that control orofacial movements. Optogenetic stimulation of CeA-to-pons axons caused excessive drinking of available liquid, regardless of palatability. When timed to the onset of bouts of licking, stimulation prolonged ingestive bout duration without affecting the number of lick bouts initiated, suggesting that this pathway modulates consummatory behaviors rather than triggering appetitive responses. Stimulation-induced overconsumption remained sensitive to visceral satiety cues, as mice eventually halted ingestion. Stimulating CeA-to-pons axons in the absence of food evoked ingestion-like motor programs including licking and chewing in the absence of any target. In a pellet grasping task, stimulation drove the overconsumption of food pellets, indicating that stimulation-induced motor programs are flexible and context-dependent. To assess the kinematic features of these motor programs, we used a machine learning-based behavioral analysis pipeline to perform automated facial tracking of mice during liquid food consumption. This revealed that while stimulation increased the number of licks, it did not impact the execution of the behavior. Taken together, these findings refine previous interpretations of CeA function, suggesting it permits overeating not solely by acting on the circuits that regulate internal need, but on the motor systems that generate ingestive behavior.

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Exercise-Induced Gut Microbiome And Metabolite Changes Reduce Sugar Consumption And Reinforcement

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Long-term exercise reduces sugar consumption and weakens gut-to-brain reinforcement signals evoked by ingested sugar, but the peripheral mechanisms underlying this effect remain unclear. We hypothesized that sustained exercise induces gastrointestinal adaptations that reshape nutrient preference. To test this, we profiled microbiome changes in mice after 42 days of voluntary exercise. Metagenomic sequencing revealed marked compositional changes in the intestinal microbiome of exercised mice maintained on standard chow. To determine whether these adaptations were required for altered food choice, we depleted the microbiome of exercised animals with broad-spectrum antibiotics. Exercised animals initially showed reduced simple carbohydrate intake, but this effect was abolished after antibiotic treatment, indicating microbiome dependence. We next tested sufficiency using fecal microbiota transplantation from exercised donors into antibiotic-treated sedentary recipients. Recipients of microbiota from exercised donors reduced sugar consumption and showed blunted nucleus accumbens dopamine responses to intragastric sugar, but not fat. Untargeted and targeted metabolomics identified secondary bile acids among the metabolites most enriched after exercise. Daily oral supplementation with secondary bile acids reduced carbohydrate intake, decreased motivated sugar seeking, and selectively attenuated dopamine responses to gut sugar infusions. Together, these findings suggest that exercise remodels the gut microbiome to increase secondary bile acid production, thereby dampening gut-to-brain sugar reinforcement and shifting nutrient choice away from sugar.

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Soluble Fiber Supplementation Prevents Perinatal High-Fat Diet-Associated Weight Gain But Not Impaired Glucose Tolerance In Rat Offspring

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Perinatal exposure to maternal high-fat (HF) diet promotes a host of physiological and metabolic consequences in offspring, such as obesity, impaired glucose clearance, hyperinsulinemia, and insensitivity to satiety hormones. β -glucan (BG), a soluble dietary fiber, is known to increase satiety by slowing gastric emptying and small intestine transit. We hypothesized that supplementing maternal HF diet with BG derived from oats would prevent perinatal HF diet-induced obesity and impaired glucose tolerance in offspring. Thirty-two pregnant female Sprague-Dawley rats on gestation day 2 were randomly assigned to three diet groups (n=10-11/diet group): chow (CH; Envigo 2018, 18% kcal fat), high-fat (HF; Research Diets D12492, 60% kcal fat), or a custom high-fat β -glucan diet (HFBG; Research Diets, 60% kcal fat, 10% oat β -glucan). Dams were maintained on these diets through pregnancy and lactation and effects on offspring were measured. There were no effects on offspring body weight at birth or postnatal day (P)7. Pups were weaned at P21. By P24, both male and female HF pups gained significantly more weight than corresponding CH (P<0.05) and HFBG (p<0.05) pups. To test glucose tolerance, P24 pups were fasted overnight for 16 h and a baseline blood sample was taken for glucose measurement. Rats were then given an intragastric gavage of glucose (2 g/kg, 20% glucose solution) prior to blood collection at 15, 30, 45, 60, and 120 minutes post-gavage. Glucose area under the curve in the HF and HFBG groups was significantly higher than in the CH group (males: p<0.01 and p<0.05 respectively; females: p<0.0001 and p=0.001 respectively). Thus, BG supplementation to maternal high-fat diet prevented weight gain in offspring, but did not improve glucose tolerance.

Chewr: An Open-Source R Package For Quantifying Chewing Efficiency

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Chewing efficiency is a measure of oral physiology that affects food breakdown and eating behavior. Existing methods to measure chewing efficiency rely on proprietary software (e.g., ViewGum) or labor-intensive procedures (e.g., sieving expectorated samples), limiting adoption and/or reproducibility. Here, we: (1) validate chewR, a user-friendly R package that quantifies chewing efficiency in a 2-color gum mixing task via automated image analysis, and (2) examine how chewR based chewing efficiency measures relate to other oral processing behaviors. Adults (n=65, 61% female) completed a test session comprised of: (1) a 2-colored gum mixing task, (2) objectively measure eating rate via Tang's carrot test, and (3) a stimulated salivary flow. Chewed gum samples were flattened with a standardized method, scanned, and resulting images were analyzed using ViewGum and chewR. Viewgum generates a ViewGum Score based on the standard deviation of the hue of the gum, with lower scores indicating better mixing. chewR produces a raw score based on hue dispersion; from this, a transformed chewR Chewing Efficiency Score is calculated, with higher values indicating greater efficiency. Chewing efficiency estimates in chewR show strong convergent validity with ViewGum Scores: the raw score and transformed Chewing Efficiency Score were each strongly correlated with ViewGum Score (r 's = 0.821, $p < 0.00001$), with signs in expected directions. For predictive validity, the transformed chewR Chewing Efficiency Score was weakly associated with carrot eating rate ($r = +0.17$), self-reported eating rate ($r = +0.27$), and stimulated salivary flow ($r = +0.16$). These findings support the use of chewR as a valid, open-source alternative to ViewGum to quantify chewing efficiency rapidly and efficiently.

Isl1+ Neurons In The Central Nucleus Of The Amygdala Are Involved In The Generation Of High Bite Force, And Coordinate The Actions Of The Jaw And Stomach During Ingestion.

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Isl1 Neurons project to brainstem regions involved in control of the jaw and the stomach. Prominent projections are observed to the parabrachial nucleus (PBN), the nucleus of the tractus solitarius (NTS), the parvocellular reticular nucleus (PCRt). Stimulation of Isl1+ neurons in the central amygdala elicited various sequences of fictive feeding. In all cases, stimulation of Isl1+ neurons in the CeA evoked biting behavior. Using a load cell to quantify biting, we observed bite force (I), number (J) and total impulse (K) was linearly related the frequency of laser stimulation ($N=3$, $P=0.00093$ bite force, $P < 0.0001$ num. bites, $P < 0.0001$ impulse). Inhibition of Isl1+ neurons, using both chemogenetic ($t(8)=4.70$, $P=0.0015$) and optogenetic ($t(4)=3.85$, $P=0.0183$) methods dramatically reduces bite force. Anatomical tracing experiments identified cells in the Mesencephalic Trigeminal Nucleus (Me5) as receiving synaptic input from CeA: Isl1+ neurons. Patch clamp recordings of Me5 neurons revealed GABA mediated excitatory post-synaptic potentials. We hypothesized that activation of CeA: Isl1+ neurons could potentiate the periodontal masseteric jaw closing reflex. We measured this reflex in urethane anesthetized animals. Laser activation significantly increases the amplitude of the masseter contraction evoked by stimulation of the teeth in the linguo-labio direction, but has no effect on stimulation in labio-linguo direction. In addition to these effects, chemogenetic inhibition of CeA: Isl1+ neurons treatment increased gastric pH ($t(3)=7.66$, $P=0.005$) in animals expecting a meal, and stimulation of Isl1+ CeA neurons suppresses the activity of the gastric antral rhythm ($t(5)=4.067$, $P=0.0097$). Subdiaphragmatic vagotomy eliminated this suppressive effect of CeA: Isl1+ neuron stimulation ($F(2,14)=1.19$, $P=0.33$).

Glp-1 Receptor Agonist Semaglutide Promotes Non-Rem Sleep And Suppresses Food/Water Intake In Naïve Rats

Elise Shealy, Patricia Sue Grigson, Jidong Fang
 Pennsylvania State College of Medicine, Hershey, PA, United States

Glucagon-like peptide 1 receptor agonists (GLP-1RAs) are prescribed for weight loss and diabetes management. Recent work in higher weight individuals with Obstructive Sleep Apnea shows that patients taking GLP-1RAs report better quality sleep. Less is known about how GLP-1RAs may affect sleep architecture. Our published data show that the GLP-1RA, liraglutide, increases Non-REM (NREM) sleep. Once-daily dosing, however, can be burdensome. Semaglutide is a GLP-1RA that is injected once-weekly in humans. Here, we test the effect of a range of doses of semaglutide, doses found effective in reducing food/water intake, body weight, and opioid seeking. Fifteen male Sprague-Dawley rats underwent electroencephalography (EEG) and electromyography (EMG) electrode implantation. They were maintained on standard laboratory chow and a 12/12 h light/dark cycle. Using a within subjects procedure, all rats were subcutaneously

(sc) injected with saline or 0.026, 0.056, and 0.078 mg/kg semaglutide using an ABA design. EEG and EMG were recorded for the 24h period following each injection, with sc injections of saline or semaglutide occurring one hour prior to dark onset; at light onset in a follow-up study. Sleep, food intake, water intake, and body weight were monitored daily. Regardless of dose, semaglutide decreased food/water intake and body weight compared to baseline measurements. Like liraglutide, semaglutide increased time spent in NREM sleep during the dark (active) cycle only, an effect that was observed even when injected at the beginning of the light (inactive) cycle. This finding suggests that timing of GLP-1RA treatment and effect on sleep quality should be considered when prescribed for weight loss, diabetes, or other conditions. This work is supported by UH3 DA030325.

P359

Pkc Δ Mediates High-Fat Diet-Induced Increased Tonic GABA_A Receptor Current In Cardiac Vagal Motor Neurons In The Dmv

Yoko B. Wang^{1,2}, Victor Q. Chen^{1,2}, Christopher D. Romero^{1,2}, Maira Jalil³, Matthew McDonald³, John N. Campbell⁴, Carie R. Boychuk^{1,2}

¹Dalton Cardiovascular Research Center, University of Missouri, Columbia, MO, United States, ²Department of Pathobiology and Integrative Biomedical Sciences, College of Veterinary Medicine, University of Missouri, Columbia, MO, United States, ³Department of Biology, University of Virginia, Charlottesville, VA, United States, ⁴Division of Food, Nutrition, and Exercise Physiology, College of Agriculture, Food and Natural Resources, Columbia, MO, United States

Intake of high fat diet (HFD) is linked to reduced cardiac vagal motor output, a main contributor to progression of cardiovascular disease. HFD for 15 days increases extrasynaptic or tonic GABA_A receptor (GABA_AR) current in cardiac projecting neurons in the dorsal motor nucleus of the vagus (CVN^{DMV}), which contributes to dampening cardiac parasympathetic output. However, the mechanism underlying this increased inhibition is unknown. We hypothesized that increased activity of protein kinase C δ isoform (PKC δ) enhances tonic GABA_AR current in CVN^{DMV} after HFD since PKC δ activation promotes GABA_AR membrane stabilization, increasing tonic GABA_AR current in neurons. Using cardiac retrograde tracing paired with whole-cell patch-clamp electrophysiology in male C57s, we found that pan inhibition of PKC activity with GFX eliminated 15-day HFD-induced increases in tonic GABA_AR current in CVN^{DMV} ($p=0.03$). Similarly, PKC δ selective inhibition with rottlerin diminished the increase in tonic GABA_AR current after HFD ($p=0.0007$), suggesting PKC δ activity mediates increased GABA_AR tonic current. Preliminary data with pHRhodo assay showed higher endocytosis in HFD. However, co-incubation with clathrin-dependent endocytosis blocker, dynasore, and rottlerin showed no difference in tonic current between NFD and HFD, suggesting that the effect of rottlerin in HFD is independent of endocytosis. We then determine the mechanism behind PKC δ increased activity. Since there were no difference in PKC δ mRNA and protein expression levels between NFD and HFD, future studies will investigate post-translational modification of PKC δ activity. Altogether, this study provides understanding on mechanisms to develop treatments targeting PKC δ for CVD related to HFD.

9:00 - 10:00 AM	Regency Foyer
Coffee Break & Exhibits	
10:00 - 11:30 AM	Millennium Hall
Oral Session 5: The 8th Sense: Interoception and Appetite	

Chair(s): Lex Kravitz

10:00

Lateralized Vagal Circuits Control Feeding

Alan de Araujo¹, Isadora Braga^{1,2}, Gabriel Tofani^{1,2}, Laryssa Coutinho¹, Mingxin Yang^{1,2}, Guillaume de Lartigue^{1,2}

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

Vagal sensory neurons in the nodose ganglia (NG) convey gut-derived signals to the brain to control eating. Despite this central role, vagal circuits have historically been considered bilaterally redundant. Emerging evidence that gut-vagal signaling can drive dopamine release through the right vagus nerve challenges this view and suggests functional lateralization. We hypothesized that left and right NG neurons (LNG and RNG) detect distinct meal-related signals and control complementary aspects of ingestive behavior. **Methods:** We combined single-nucleus RNA sequencing, behavioral assays, and brain-wide activity mapping in mice. **Results:** snRNA-seq of nodose neurons revealed widespread transcriptional asymmetry between LNG and RNG, with chemosensory-enriched cells biased toward the RNG and mechanosensory-enriched cells biased toward the LNG. Restricting analysis to gut-innervating neurons preserved this organization, indicating that laterality is embedded within intestinal vagal circuits. Chemogenetic stimulation and caspase-mediated ablation revealed that the RNG, but not LNG, was necessary and sufficient for fat-associated memory recall after memory decay. Conversely, the LNG, but not RNG, was necessary and sufficient to induce distension-induced satiety and suppress subsequent intake. Consistently, optogenetic stimulation of LNG and RNG neurons recruited distinct central circuits: RNG stimulation significantly increased hippocampal activity, whereas LNG stimulation activated hypothalamic nuclei involved in homeostatic feeding control. **Conclusion:** This work identifies functionally specialized, lateralized vagal NG populations that differentially encode meal-related signals and provides a mechanistic framework for how gut-derived signals guide ingestive behavior.

10:15

Molecular Mechanisms For Sensing Stomach Distension

Avnika Bali^{1,2}, Isadora Braga^{1,2}, Guillaume de Lartigue^{1,2}

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

Gut distension signals give rise to feelings of fullness and meal termination as well as parasympathetic processes such as gastric emptying, gut motility, thermoregulation and glucose homeostasis. Vagal afferent neurons (VANs) are known to respond to diverse mechanical signals in the gut and suppress feeding. Mechanical forces including tension, relaxation, pressure and flow likely require specialized mechanoreceptors and may be conveyed through distinct neuronal pathways, but the molecular mechanisms that transduce these mechanical stimuli are poorly defined. We therefore hypothesized that a heterogeneous class of mechano-transducers define separate mechanosensory populations that affect disparate behavioral and physiological processes. Results: Using in vivo Ca²⁺ imaging combined with multiplexed FISH in mice with intragastric balloons, we identified Piezo2 and TRPA1 as candidate mechanosensitive ion channels expressed in non-overlapping populations of stretch-responsive VANs. These populations are distributed across canonical receptor-defined vagal subtypes, including Glp1r- and Oxt-expressing neurons. To directly test function, we selectively deleted Piezo2 or TRPA1 in stomach-innervating VANs. Loss of either channel contributes towards distension-induced reduction in food intake and locomotion. In contrast, only Piezo2 was required for distension-induced autonomic responses. All experiments were performed in mice (n= 5-8 per group). Conclusions: These findings identify Piezo2 and TRPA1 as key molecular transducers of gastric distension in distinct vagal mechanosensory populations, revealing parallel pathways that differentially regulate behavioral and autonomic components of eating and homeostasis.

10:30

Encoding Of Interoceptive State By Paraventricular Thalamic Ensembles

Jared Butts¹, Samuel Congdon^{1,2}, Vraj Patel¹, Qingyin Zheng², Patrick Sweeney^{1,2}

¹Neuroscience Program, University of Illinois Urbana-Champaign, Urbana, IL, United States, ²Department of Molecular and Integrative Physiology, University of Illinois Urbana-Champaign, Urbana, IL, United States

Organisms must constantly assess internal state and external stimuli to identify need state and drive motivated behavior. The paraventricular nucleus of thalamus (PVT) is a midline thalamic structure known to integrate interoceptive and exteroceptive cues and promote ingestive behavior via its connectivity with canonical homeostatic centers. However, the population and single-neuron level encoding of homeostatic perturbations within the PVT have yet to be fully described. Here, we utilized a pan-neuronally expressed calcium indicator combined with in vivo microendoscopy in behaving animals (n=12 C57BL/6J mice, 6 male & 6 female) to longitudinally characterize PVT responses to diverse homeostatic challenges. In a multisession fast-refeeding paradigm, we identified three stable responses to chow: neurons that are 1) highly active in the fasted state and inhibited by food consumption, 2) transiently activated during consumption, and 3) activated following the bulk of consumption. Internal state and food palatability modulate PVT encoding of ingestion, as pretreatment with semaglutide attenuated chow responses while high fat diet increased their magnitude. These responses are stable across need states, as the consumption of a liquid diet in the fasted state and water following water deprivation induced similar responses at the individual cell level. Consistently, neurons that exhibited increased activity in the fasted and thirsty state were activated by acute cold exposure, while neurons that increase activity during a refeed and water access were inhibited by cold, indicating selective tuning to state and stimulus valence. Thus, we have identified a unique homeostatic nucleus that bidirectionally encodes valence across vastly different behaviors and states.

10:45

Urocortin-3 Suppresses Food Intake And Intestinal Inflammation Via An Enteroendocrine Gut-Brain Circuit

Giulia T. Uhr^{1,2,3}, Lavinia Boccia^{2,3}, Niklas Blank^{4,5}, Timothy O. Cox¹, Lenka Dohnalová¹, Haohan Karen Wei¹, Kaitlyn McElhern^{2,3}, Carol Rau^{2,3}, Stephen Wisser¹, Leonel Joannas^{6,7}, Jorge Henao-Mejia^{6,7}, Maayan Levy^{4,5}, J. Nicholas Betley^{2,3}, Christoph A. Thaiss^{4,5}

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Intestinal enteroendocrine cells (EECs) sense luminal signals and regulate whole-body physiology. Whether EECs also play a role in the regulation of intestinal inflammation and responses to infection remains unclear. We hypothesized that activation of irritant-sensing EECs engages a gut-brain pathway that suppresses food intake and protects against intestinal inflammation. Using mice, we combined chemogenetics, peptide administration, colitis models, organoid culture, and neural activity mapping to characterize this gut-brain circuit linking nutrient sensing to the regulation of feeding and intestinal immunity. Activation of the irritant receptor TRPA1 in EECs increased release of urocortin-3 (UCN3), a ligand for CRHR2-expressing vagal afferents. Activation of this pathway suppressed hypothalamic AgRP neuron activity and reduced food intake, thereby lowering inflammatory monocyte infiltration. In dextran sulfate sodium-induced colitis, UCN3 signaling decreased inflammatory monocyte infiltration and improved disease outcomes, whereas genetic or chemogenetic disruption of UCN3–CRHR2 signaling exacerbated inflammation. Importantly, UCN3 reduced feeding without inducing aversive malaise behaviors, in contrast to classical anorectic pathways. Mouse treatment groups ranged in size from n = 3 to 12. Statistical analyses included unpaired two-tailed t-tests or ANOVA with post hoc comparisons, with significance set at p < 0.05. These findings identify a previously unrecognized EEC-mediated gut-brain circuit that links nutrient sensing to the coordinated regulation of feeding and intestinal immunity. This pathway may represent a new therapeutic target for obesity and inflammatory bowel disease with reduced adverse effects compared to existing treatments.

11:00

Associations Between Interoceptive Awareness And Appetitive Traits In Children With Overweight Or Obesity (New Investigator Travel Awardee)

Allison M. Boyar^{1,2}, David R. Strong³, Kyung E. Rhee⁴, Kerri N. Boutelle^{2,3,4}

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Interoceptive awareness (IA), the ability to perceive bodily signals, regulates eating behavior. We hypothesized increased IA of internal cues would be associated with stronger satiety responsiveness (SR) and weaker reactivity to external food cues in children with overweight or obesity (OW/OB). 121 children (mean age = 10.65 ± 1.66 years; mean %BMI_{p95} = 112.11 ± 13.88 ; 68.6% female; 48.8% White, 25.6% Hispanic/Latino, 25.6% other) counted self-perceived heartbeats during 3 intervals compared to electrocardiogram recording. Concordance scores ranged from 0-1 (higher = better IA). Parents reported child eating behaviors via Eating in the Absence of Hunger and Child Eating Behavior questionnaires. Regression models adjusted for child and parent demographics, %BMI_{p95}, and parent BMI when estimating associations of IA with reactivity to internal (SR; NAE: negative affect eating) and external cues (FR: food cue responsiveness; EE: external eating). In support of hypotheses among children with mid-range levels of IA, higher IA was associated with lower levels of FR ($b = -3.40, p = .001$) and EE ($b = -2.42, p = .011$). However, children with the highest levels of IA had lower levels of SR ($b = -2.53, p = .035$) and higher levels of FR ($b = 3.54, p = .012$) and EE ($b = 2.75, p = .035$). No associations were observed between IA and SR, NAE, FR or EE within the lowest range of IA ($ps > .149$). Moderate IA may represent an optimal regulatory range, buffering reactivity to external food cues. High IA may reflect true sensitivity, attentional bias, or misattribution of internal signals when assessing satiety and may heighten learning of salient food cues. IA may be a modifiable target when addressing overeating driven by appetitive traits in children with OW/OB.

11:15

Evaluation Of A Two-Stage Water Loading Test To Measure Gastric Interoception In Children

Emily Hohman, Orfeu Buxton, Kathleen Keller
Penn State University, University Park, PA, United States

Individual differences in interoception (internal state sensing) may contribute to obesity risk, but objective measures are limited. We evaluated the two-stage water loading test (WLT-II) as a measure of gastric interoception in children and related this measure to the Multidimensional Assessment of Interoceptive Awareness-Youth (MAIA-Y) and Interoception Sensory Questionnaire (ISQ) measures. In stage 1 (satiation), 7–10-year-olds ($n=53$) were instructed to drink water from an opaque bottle through a straw until they felt as if they had eaten ‘just enough’; in stage 2 (fullness), they drank additional water until completely full. The volume of water to reach satiation as a percentage of total volume consumed (%sat) is an index of gastrointestinal interoception that is independent of stomach volume; higher %sat reflects poorer interoception. Children drank 125 ± 88 ml (mean $\pm$ SD) in stage 1 and 136 ± 93 ml in stage 2; %sat was $48 \pm 15\%$ (range 17-82%). Mean %sat was higher in girls than boys (52 vs. 45%, $p=0.06$) and in younger (7-8) vs. older (9-10 years) children (54 vs. 45%, $p=0.03$). Greater interoceptive difficulty (ISQ) was associated with higher %sat in the full sample ($r=0.26, p=0.06$) and among older children ($r=0.40, p=0.02$). Among older children only, MAIA-Y Noticing Body Sensations was negatively associated with %sat ($r=-0.39, p=0.03$). MAIA-Y Body-Listening was associated with lower %sat ($r=-0.37, p=0.06$) in girls, but was unexpectedly associated with higher %sat ($r=0.44, p=0.03$) among boys. The WLT-II is feasible in children and correlates with self-report measures of interoception, though not all in expected directions. Future analyses will examine associations between %sat and cardiac interoception, eating behaviors, and adiposity.

Oral Session 6: Molecules that Matter: Neuropeptides & Feeding

Chair(s): Christelle. LeFoll

10:00

Central Amygdala Glucagon-Like Peptide 1 Receptor Neurons Integrate Endogenous Glp-1 And Encode Consummatory Valence Through Diverse OutputsMiguel Duran¹, Jennifer Willis¹, Sai Pochana¹, Nilay Dalvi¹, Anusha Polamarasetty¹, Melissa Rodriguez¹, Kirk Habegger², J. Andrew Hardaway¹¹Department of Psychiatry and Behavioral Neurobiology, University of Alabama at Birmingham, Birmingham, AL, United States, ²Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, United States

Pharmacotherapies targeting GLP-1 receptors (GLP-1Rs) are transforming diabetes treatment. Despite the rapid adoption of GLP-1 analogs in the clinic, our understanding of the endogenous GLP-1 and GLP-1R system, particularly in the limbic system, has not kept pace. We used *Glp1r*-Cre; *Gcg*-FlpO mice to label GLP-1R neurons in the central amygdala (CeA, *Glp1r*^{CeA}) and GLP-1-producing neurons in the nucleus of the solitary tract (*Gcg*^{NTS}) with eGFP and TdTomato respectively. We then used tissue clearing combined with light sheet microscopy to quantify proximity of *Glp1r*^{CeA} soma to *Gcg*^{NTS} axons and whole brain outputs of *Glp1r*^{CeA} and *Gcg*^{NTS} neurons. We identified *Glp1r*^{CeA} axons in thalamic, hypothalamic, midbrain, and brain stem nuclei. Using optogenetic-assisted mapping in *ex vivo* brain slices and electrophysiology, we detected functional inhibitory connections in a subset of these nuclei. Within the CeA, *Glp1r*^{CeA} neurons inhibit >50% of recorded medial CeA (CeM) cells and bath application of GLP-1 enhances this inhibition. We then used immunofluorescence to detect GLP-1R protein on CeM neurons. Consistent with the presence of GLP-1R protein in the CeA, bath application of GLP-1 resulted in persistent inward currents and significant depolarization. Using fiber photometry in *Glp1r*^{CeA} neurons, we observed the activation of these neurons in response to aversive stimuli, tastants, or ramping during appetitive behavior. Food consumption; however, was coupled with a significant decrease *Glp1r*^{CeA} neuron activity. Finally, we used chemogenetic inhibition and observed that activation or inhibition of *Glp1r*^{CeA} neurons reduced or increased high fat diet consumption respectively. We conclude that *Glp1r*^{CeA} neurons integrate endogenous GLP-1 inputs and serve as a brake on palatable food intake.

10:15

Top Down Regulation Of Feeding And Body Weight By Mc4R In The MpfMichaela Cooke¹, Priyanka Das¹, Maddy Smith¹, Rachel Ross^{1,2}¹Albert Einstein College of Medicine, Bronx, NY, United States, ²Montefiore Medical Center, Bronx, NY, United States

Body weight (BW) maintenance depends on coordinated regulation of feeding, locomotion, thermogenesis, and baseline energy use involved in autonomic regulation. Clinical studies implicate medial prefrontal cortex (mPFC) dysfunction in obesity and in eating disorders across the weight spectrum, but the functional roles of its subregions in feeding and energy balance remain poorly defined. The melanocortin-4 receptor (MC4R), a brain-expressed GPCR critical for energy homeostasis, has been studied primarily in hypothalamic circuits. Here, we hypothesize MC4R functions differently in dorsal and ventral mPFC subregions in response to metabolic state change, as we found that expression of the peptide varies with satiety. Using region-specific deletion in male MC4Rlox/lox mice, with data analyzed by ANOVA with multiple comparison tests, we find opposing effects on BW: loss of MC4R in ventral mPFC (vmPFC) increases BW (n=15), whereas deletion in dorsal mPFC (dmPFC) decreases BW (n=12) compared to controls. However, both manipulations reduce fasted-state locomotion with no change in fed state. Preliminary calorimetry suggests dmPFC MC4R signal promotes energy expenditure in male mice, while vmPFC MC4R signal favors energy conservation in both sexes. Consistent with this, dmPFC MC4R neurons preferentially project to locomotor and effort-related regions (medullary pyramids, periaqueductal gray), whereas vmPFC MC4R neurons target circuits regulating consummatory behavior (lateral septum, medial preoptic area, substantia innominata, nucleus accumbens shell). Together, these findings indicate that MC4R signaling in distinct mPFC subregions oppositely regulates energy balance through separable behavioral and circuit mechanisms which may play a role in disordered eating and body weight.

10:30

Glp-1R Agonism Modulates Lipid-Induced Neutrophilia Via An Area Postrema-Independent MechanismAnna Parolini¹, Sophia Fischer², Tito Borner², Giuseppe Danilo Norata¹, Andrea Baragetti¹¹Department of Pharmacological and Biomolecular Sciences, University of Milan, Milan, Italy, ²Department of Biological Sciences, University of Southern California, Los Angeles, CA, United States

High-fat diet (HFD) feeding induces metabolic dysfunction and systemic inflammation. Transitions between fasting and feeding, which engage GLP-1R signaling, trigger rapid metabolic shifts that subsequently activate inflammatory immune responses. However, whether GLP-1R signaling links nutrient ingestion to postprandial immune-inflammation, and through which mechanism, remains unknown. Here we tested whether GLP-1R activation impacts innate immune-inflammation during acute and chronic HFD challenges and whether this effect is mediated by the area postrema (AP), a key hindbrain node for GLP-1 signaling. To assess GLP-1R signaling impact on lipid-induced postprandial immune-inflammation, Sprague-Dawley rats were fasted overnight and then subjected to intragastric fat gavage two hours after pretreatment with semaglutide (10nmol/kg). Blood immunophenotyping was performed in both chow- (n=8/group) and HFHS-fed (45% kcal from fat, 20% kcal from carbs; n=4/group) rats. To evaluate AP-mediated immunometabolic modulation, rats underwent AP lesion (APX; n=8) or sham surgery (n=8), followed by acute HFD refeeding post-fasting. A single fat gavage in prominent increase in circulating neutrophils versus controls, while semaglutide pretreatment attenuated acute lipid-induced circulating neutrophilia in both chow- and chronic HFHS-fed rats. In APX rats undergoing acute HFD refeeding, neutrophilic responses matched those of sham-operated controls. GLP-1R activation modulates fat-induced neutrophilia independently of the area postrema. We propose GLP-1 as a novel potential regulator of immunity beyond its metabolic actions, highlighting immunometabolic crosstalk whereby GLP-1 could bridge systemic metabolism and postprandial innate immune responses.

10:45 **Effects Of *Gcg*-Derived Peptide Signaling On Body Composition And Caloric Intake**

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

Western diets (WD) tend to be calorically dense, relatively high in fat and sugar, and relatively low in protein, all of which likely contribute to WD-induced increases in obesity and metabolic disease. The glucagon gene (*Gcg*) encodes preproglucagon, which is cleaved into glucagon-like peptide-1 (GLP-1) and related peptides that regulate appetite and energy balance. While synthetic GLP-1 receptor agonists suppress WD intake and BW, the role of endogenous GLP-1 and related peptides remains unclear. We used genetic knockdown (KD) of *Gcg* to disrupt preproglucagon-derived peptide signaling and assess effects on food choice, caloric intake, and body composition in rats. EchoMRI was conducted before and after 8 weeks of diet exposure. At 6wks of age, male and female KD and wild-type (WT) rats were group-housed and assigned to chow (C) alone (Lab Diet 5001) or to a choice of C and WD (Research Diets D12079B) for 8 wks. Average kcal intake per cage of group-housed rats was calculated weekly and compared between the two diet conditions, and separately within the C+WD choice groups. KD rats of both sexes consumed significantly more kcal and gained significantly more BW than WT rats, with an additional main effect of diet on BW gain and a trending effect of diet on kcal intake in females. WD-fed KD rats gained significantly more fat mass than WD-fed WT rats. For rats in the food choice group, male KD rats consumed more WD-derived kcals than WT males and showed a greater preference for WD vs. C; a similar trending effect of genotype was seen in females. These findings demonstrate that endogenous *Gcg*-encoded peptide signaling is linked to increased food intake and fat mass in rats, with some apparent sex differences.

11:00 **Primary Cilia *Adcy3* Is Necessary For *Dmvmh* Leptin Effects On Feeding**

Christopher Petty¹, Austin Mills², Magen Lord², Ruth Harris³, Emily Noble^{1,2}

¹Neuroscience Graduate Program, University of Georgia, Athens, GA, United States, ²Department of Nutritional Sciences, University of Georgia, Athens, GA, United States, ³Department of Physiology, Augusta State University, Augusta, GA, United States

Leptin acts in the dorsomedial ventromedial hypothalamus (dmVMH) to reduce food intake, but this function of leptin is reduced in obesity. Neurons in the dmVMH contain primary cilia, which are organelles that contain concentrated G protein-coupled receptors whose signals are transduced via adenylyl cyclase type 3 (ADCY3). Leptin increases ADCY3 in the hypothalamus, and ADCY3 signaling necessary for anorexigenic responses of some hypothalamic neuropeptides. Whether leptin modulates ADCY3 in the dmVMH and/or requires ADCY3 to modulate food intake in this region is unknown. We hypothesize that leptin increases primary cilia ADCY3 in the dmVMH, and that ADCY3 is necessary for leptin mediated food intake reductions. Our results in male Sprague Dawley rats show that peripheral leptin administration at dose effective for reducing food intake elevates pSTAT3 in dmVMH primary cilia containing neurons and increases ADCY3 positive ciliary length and number (n=8/group; Student's t-test; P<0.05). To determine whether ADCY3 is necessary for leptin mediated reductions in food intake, virogenetic knockdown of ADCY3 was used. ADCY3 knockdown in the dmVMH increased food intake and body weight (n=12/group; Two-way ANOVA, Fishers LSD; P<0.05), with no differences in energy expenditure in male SD rats. Leptin in the dmVMH reduced food intake in control animals, but not in animals with ADCY3 knockdown, suggesting that ADCY3 is necessary for leptin-mediated food intake reduction. Our findings provide mechanistic insight for how leptin signals to reduce food intake and may be important for understanding how the effectiveness of leptin is impacted by internal state.

11:15 **Neuropeptide Y1 Receptor-Expressing Neurons In The Paraventricular Hypothalamus Link Hunger And Reward Circuits To Drive Feeding**

Sam Z Bacharach¹, Katie A Zappetti^{1,2}, Laryssa O Coutinho¹, Zhongwu Liu³, Marcelo O Dietrich³, Amber L Alhadeff^{1,2}

¹Monell Chemical Senses Center, Philadelphia, PA, United States, ²University of Pennsylvania, Philadelphia, PA, United States, ³Yale School of Medicine, New Haven, CT, United States

Agouti-related protein (AgRP)-expressing neurons in the arcuate nucleus are tuned to hunger state and are critical for feeding behavior. Stimulation of AgRP neurons robustly drives food intake and increases nucleus accumbens (NAc) dopamine (DA) release to food. However, the circuit mechanisms linking AgRP

neurons to mesolimbic DA remain poorly understood, limiting our ability to explain how hunger governs food-driven motivation. We first tested whether AgRP neuron activation alters synaptic input onto ventral tegmental area (VTA) DA neurons. Chemogenetic excitation of AgRP neurons in mice (n=12) decreased IPSC frequency in VTA DA neurons, suggesting a decreased inhibitory tone onto VTA DA neurons. This provides a synaptic mechanism by which hunger enhances DA responses to food. AgRP neurons do not project directly to the VTA, so to identify the circuit mechanisms connecting the two, we optogenetically stimulated seven major AgRP projection targets while recording DA release in the NAc (n=75). Stimulation of AgRP terminals in the paraventricular hypothalamus (PVH) phenocopied AgRP cell body activation, robustly increasing DA release to food and driving feeding. Because AgRP neurons co-release NPY, we hypothesized that AgRP neurons inhibit Y1 receptor-expressing (Y1R) neurons in the PVH to reduce inhibitory tone onto VTA DA neurons. We used RNAscope and in vivo calcium imaging to show that AgRP neuron activation suppressed PVH Y1R neuron activity (n=14). Moreover, DREADD-mediated inhibition of PVH Y1R neurons increased NAc DA release to food and promoted feeding (n=9). We used ANOVA with post hoc t-tests to analyze all data. Together, these findings identify PVH Y1R neurons as a critical intermediary connecting hunger signals to mesolimbic DA circuits to promote feeding.

11:30 - 1:00 PM	On Own
Lunch on Own	

11:45 - 12:45 PM	Regency B
New Investigator Event - Meet the Scientist	

Meet and speak with scientists representing academia, industry, and research institutions in an informal setting. This is a great opportunity to ask questions, make connections, and learn about a range of scientific careers and research experiences.

[Register Here.](#)

1:00 - 2:00 PM	Millennium Hall
Mars Lecture 3: Daniella Cota	

Chair(s): Thomas Lutz

1:00

Understanding Pomc Neurons Heterogeneity In Energy Balance And Beyond

Daniela Cota

INSERM, Neurocentre Magendie, U1215, University of Bordeaux, Bordeaux, France

Hypothalamic pro-opiomelanocortin (POMC) neurons are critical regulators of energy balance. By integrating adiposity and nutrient signals, they classically act to restrain food intake and promote energy expenditure via melanocortin signaling. Genetic disruption of POMC in mice and humans produces hyperphagia and severe, early-onset obesity, underscoring that intact POMC neuron function is indispensable for defending against positive energy balance and obesity pathogenesis. Nevertheless, recent evidence demonstrates that POMC neurons are molecularly and functionally heterogeneous, can stimulate feeding under specific conditions, and become active before food consumption, therefore challenging the traditional view of their satietogenic function. Here I will present published and unpublished data we have generated illustrating the complex roles of hypothalamic POMC neurons in energy balance and beyond.

2:00 - 3:00 PM	Regency A
Poster Session 5-1	

P302

Non-Linear Estimates Of Nutritional Properties, Driven By Health Biases, Lead To Systematic Errors In Caloric Food Choice

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Maintaining a daily caloric deficit while dieting underlies most successful weight loss programs. Accurate estimation of caloric content is central to effective dietary regulation, yet most everyday food choices rely on subjective judgments rather than labeled nutritional information. We investigated whether these judgments are systematically biased and how such biases influence caloric decision-making. In Experiment 1, 247 online participants estimated the caloric and macronutrient content of 68 photographed foods. Across nutrients, subjective estimates were better characterized by a logarithmic than a linear function of objective nutritional values ($F=78$, $p<0.001$), suggesting Weber–Fechner–like magnitude compression. Additionally, the degree of non-linearity scaled with each nutrient’s association with perceived healthfulness ($q=0.79$, $p<0.05$); caloric estimates were most strongly correlated with healthfulness judgments ($r=-0.92$, $p<0.001$). In Experiment 2, 157 participants completed a forced-choice task selecting the higher-calorie item from pairs of foods that differed by ~200 kcal or ~100 kcal. Choice accuracy declined as the average caloric magnitude of food pairs increased (logistic regression: $\beta=-0.73$, $p<0.001$), consistent with the magnitude compression model. Critically, errors were disproportionately driven by “health conflict” trials, in which perceived healthfulness opposed actual caloric differences ($\beta=-1.95$, $p<0.001$). Participants who relied more heavily on perceived healthfulness were significantly less accurate overall ($r=-0.63$, $p<0.001$). Together, these findings demonstrate that caloric judgments are shaped by both psychophysical compression and healthfulness heuristics. When caloric discrimination becomes difficult, particularly among calorie-dense foods, individuals substitute health-based impressions for objective magnitude computations,

leading to systematic and predictable errors. Such biases may contribute to everyday misestimation of energy intake with cumulative consequences for weight regulation.

P304 **Satiety Insecurity Is Associated With Diet Quality Of Foods Selected By Women From An Online Grocery Store Task**

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Food insecurity is associated with obesogenic eating behaviors, including overeating and poorer diet quality. Satiety insecurity—worries about maintaining fullness—has been proposed as a pathway linking food insecurity to larger portion sizes and higher BMI, particularly among women. However, it is unclear whether satiety insecurity influences quality of dietary choices and explains the relationship between childhood food insecurity and diet quality in adulthood. We examined this question in an online study of 596 U.S. women of childbearing age ($M\text{ Age} = 32 \pm 7$), who completed measures of childhood and past-year food insecurity, and satiety insecurity. Participants also completed an online grocery shopping task where they selected all foods they would eat for seven days from a platform simulating a major U.S. grocery retailer. Diet quality was computed with the Healthy Stars profiling system, such that foods were scored as healthier when categorized as produce, nutrient-rich, high in fiber, or less processed. Higher satiety insecurity was associated with selecting foods with worse diet quality, adjusting for food insecurity ($B = -0.46$, 95% CI: $-0.90, -0.03$). There was also a significant indirect effect: greater childhood food insecurity predicted higher satiety insecurity, which in turn predicted poorer diet quality, even after controlling for past-year food insecurity (Indirect Effect = -4.42 , 95% CI: $-9.33, -0.88$). These findings indicate that concerns about maintaining fullness influence food choice and diet quality, not only portion size, and support satiety insecurity's role as a mechanism linking early-life food insecurity to persistent obesogenic eating patterns.

P306 **Moderate To Vigorous Physical Activity As A Cause Of Reduced Relative Energy Intake In Women With Loss Of Control Eating**

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In healthy populations, moderate to vigorous physical activity (MVPA) reduces relative energy intake (REI); this effect is larger when MVPA occurs in a fasted state. It is unknown if MVPA reduces REI in individuals with loss of control eating or what mechanisms underlie these effects. We hypothesized that MVPA would reduce 24-hr REI compared to rest and that engaging in MVPA in a fasted, compared to fed, state would reduce 24-hr REI. Data come from an ongoing trial. Eleven women with loss of control eating completed three conditions in a counterbalanced order: ate breakfast and engaged in 30 min of MVPA at 75% $\dot{V}O_{2\text{max}}$ (fed state), ate breakfast and abstained from MVPA (rest), and abstained from breakfast and engaged in 30 min of MVPA at 75% $\dot{V}O_{2\text{max}}$ (fasted state). Participants completed assessments of posited mediators: plasma for ghrelin and a progressive ratio task to assess food reward value. Food intake was objectively measured for the 24-hr period. MVPA in the fed state did not reduce REI compared to rest ($t(10) = -.57$, $p = .58$, $d_z = -.17$). MVPA in the fasted state trended toward reduced REI compared to MVPA in the fed state ($t(10) = -1.92$, $p = .08$, $d_z = .58$). Removing two outliers who likely engaged in binge eating, MVPA caused a large reduction in REI ($t(8) = -.50$, $p = .001$, $d_z = -1.68$). In the subset of ghrelin samples that have been assayed; we observed a moderate decrease in ghrelin in the fed MVPA condition compared to rest ($t(3) = -1.37$, $p = .26$, $d_z = .69$). MVPA compared to rest did not change food reward value ($t(10) = -.45$, $p = .67$, $d_z = .14$). Preliminary results suggest that MVPA does not reduce REI in all women with loss of control eating. A larger sample is needed to investigate heterogeneity in the effects of MVPA on energy intake and binge eating.

P308 **Factors Associated With Weight Loss Success: An Umbrella Review And The Delta Grid Taxonomy**

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Decades of research on weight loss determinants have produced a fragmented literature; no synthesis has exposed where systematic blind spots lie. One-dimensional taxonomies cannot simultaneously distinguish where a determinant resides and how it operates. Hypothesis: A two-dimensional umbrella synthesis would expose systematic blind spots—empty cells reflecting research traditions, not absent phenomena. Species: Human. Subjects: 49 systematic reviews from 1,118 primary studies ($n \geq 700$ each) and 138,153 adults attempting weight loss. Procedures: PRISMA 2020 umbrella review; dual-independent screening; adapted AMSTAR-2. 286 raw factor mentions were consolidated to 96 unique factors via established frameworks. From this synthesis we built the DELTA Grid: 5 (Locus: BIO/PSY/HAB/REL/ENV) $\times$ 4 (Mechanism: Affective/Behavioural/Cognitive/Desire). Two coders classified factors independently; Cohen's $\kappa = 0.58$ – 0.78 . Results: The Grid exposed systematic blind spots, not balanced coverage. Six of 20 cells (30%) were empty, including BIO $\times$ Affective and the entire REL $\times$ Cognitive/Desire row. Behavioural mechanisms dominated (50%); affective lever sparse (11.5%); relational domain marginal (3.1%). AMSTAR-2 confidence was low in 66.0% of reviews. Cross-review overlap: 1.1%, indicating independent convergence on the same biased map. Conclusions: The umbrella-derived DELTA Grid shows that the weight management evidence base is not a balanced map of reality but reflects research traditions. The exposed blind spots—relational and affective-biological intersections—offer a clear research agenda: targeted primary studies where evidence is absent. The Grid serves as a directional guide for new research and clinical screening of weight-loss barriers.

P310 **Different Psychological And Cognitive Processes Are Implicated In The Motivation To Work For Food Compared To Monetary And Game Play Rewards. (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))

Cassandra J. Lowe

University of Exeter, Exeter, United Kingdom

A crucial aspect of human eating behaviours is that it requires a certain degree of motivation or willingness to exert effort towards seeking, obtaining, and consuming the food item. Motivation is a complex behaviour that is not easy to quantify in humans, and researchers are often required to infer motivation from invested effort. The underlying assumption of this premise is that the magnitude of the invested effort an individual is willing to exert will depend largely on the assigned value of the reward. Here, we assessed whether different psychological and cognitive processes are implicated in the motivation to work for food rewards compared to monetary or game play rewards. A sample of 530 participants aged 18-47 ($M=23.69$; $SD = 4.34$; 52.8% women) were randomly assigned to one of three reward conditions: (1) food-reward ($n=177$); (2) monetary rewards ($n= 179$); (3) game play rewards ($n=174$). In each condition, participants completed a progressive ratio task for chocolate candies (food reward), money, or game (Mario Kart) play time (game play reward). Prior to the PR task condition, participants completed a series of cognitive tasks, measures of impulsivity, and eating pathology. Results from the network analyses revealed that the food reward motivation is driven largely by temporal discounting for food rewards and binge-eating pathologies. Whereas motivation for game play rewards is driven by sensation seeking, and monetary rewards by temporal discounting. These findings suggest that the psychological and cognitive processes that predict motivation to work for food rewards are distinct from other primary rewards.

P312

Comparing Habituation Responses To Hyperpalatable Foods In Children

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Habituation is a process in which repeated exposure to a stimulus results in a diminished response to that stimulus. Habituation has been used to explain how sensory stimuli influence food choices and consumption, and is a mechanism to explain a gradual decrease in response during a meal. Hyperpalatable foods (HPF) are foods that contain combinations of macronutrients at high thresholds that are designed to maximize the reinforcing value of a food. HPFs are defined by their macronutrient composition including fat-sodium, fat-sugar and carb-sodium, as well as allowing for classification into multiple categories. Using a sample of 8-12-year-old children ($n=231$), we examined habituation to snack foods meeting all HPF categories (HPF-all) to a second snack food in each category in a mixed design. Using mixed effect regression analysis, we compared foods meeting all criteria (fat, sodium, sugar and carbohydrates; HPF-all) to fat-sodium, carb-sodium and fat-sodium-carb foods on change in rate of responding for food over 24-minutes as an index of habituation. ANOVA was used to compare total responses for food as an index of motivation. In the mixed-effect regression, carb-sodium HPFs had significantly faster habituation than HPF-all ($p=0.002$), but there were not differences in habituation for fat-sodium or fat-sodium-carb HPFs. In the ANOVA, HPF-all category had significantly greater total responding compared to fat-sodium and fat-sodium-carbohydrate ($p<0.05$), but not carbohydrate-sodium ($p=0.053$) This research suggests greater levels of HPF slow habituation compared to carb-sodium HPFs and that greater macronutrient combinations may slow habituation and potentially increase motivation to consume those foods. Future research should examine how hyperpalatable foods can affect habituation and energy intake.

P314

Comparison Of Food Nova Scores With And Without Contextual Data.

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As the average American diet shifts to encompass a greater percentage of processed foods, it is increasingly important to use methods that integrate food processing classifications into dietary recall assessment. The Nova system, the most widely used food processing classification system, is best equipped to classify foods with contextual data (e.g. brand, store, ingredients); however, in many traditional dietary recalls methodologies and large data sets, contextual data is not captured and is cumbersome to collect. Here, we aim to inform best practices by determining the impact and necessity of contextual data for Nova scoring accuracy. We hypothesize that Nova classification performed with contextual data will result in greater classification accuracy and inter-rater reliability compared to classification performed without contextual data. In a recent pilot study ($n=28$, age: 37.5 ± 14.7 years), 24-hour dietary recalls were collected using Nutrition Data System for Research software. A total of 734 foods were captured, and participants (82% female, 92% white) consumed 204.4 ± 66.5 g/d of carbohydrates, 76.1 ± 22.4 g/d of fat, 78.4 ± 20.5 g/d of protein. Three independent raters will Nova classify food entries across dietary recalls with two methods: 1) through the creation of a data dictionary in which each unique food is Nova scored one time without additional contextual data and 2) each food will be individually classified with contextual data. Inter-rater reliability will be assessed with intra-class correlation from a two-way mixed effects model using the consensus from the three raters. Comparing these two methods will clarify tradeoffs between accuracy and speed of data collection/analysis, informing interpretation of population-level studies.

Sensory Processing In Children With And Without Feeding Problems: Examination Of Subgroups Differences

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Sensory processing in children with and without feeding problems: Examination of subgroups differences

Rationale: Studies have described relations between sensory processing and feeding problems but few studies have included children identified with feeding problems. While studies found differences in feeding and sensory problems (SP) between children with autism spectrum disorder (ASD) and neurotypical development (NT), few have examined sensory and feeding problems in children with other forms of neurodevelopmental disorders such as attention deficit hyperactivity disorder (ADHD) or Intellectual disability (ID). This study extends the current research by examining differences in SP related to feeding in subgroups of children with neurodevelopmental disorders (NDD) and children with NT in a sample referred to a feeding clinic. **Hypotheses:** Children with ASD and ID, who presumably have more neurological involvement, than children with NT, ADHD, speech delay, reading disorder, or learning disability will have more SP problems. Children with NT referred to a feeding clinic score higher on a measure of SP problems than children with NT and without feeding problems. **Subjects:** 546 children with feeding problems, 316 control children **Methods:** ANOVAs with Bonferroni post hoc tests were conducted to compare the mean scores on a SP measure (SEPS-R) and its subscales for subgroups of children with ASD, ID, ADHD, speech delay, RD, or LD, and NT. **Results:** Consistent with the hypotheses, ASD and ID groups scores significantly higher on the total scores and all subscale scores when compared to the NT group. **Conclusions:** The presence of an identified feeding problem did not mitigate the differences between children with ASD or ID and children with NT or other NDDs.

P320

A Novel Approach To Target The Tongue For Drug Delivery Of Obesity Therapeutics

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Obesity remains a global health burden and recently an abundance of research has been dedicated to combating this disease. Glucagon-like peptide-1 (GLP-1) receptor agonists have been at the forefront of obesity treatment, with many other neuroendocrine and incretin hormones being explored. Current therapeutics are primarily injectables and associated with adverse gastrointestinal side effects, contributing to discontinuation of treatment. Thus, alternative administration routes are needed. Here, we investigate the oral cavity, particularly the tongue, as a potential site for targeted drug delivery. Taste-bud cells (TBCs) located on the tongue detect and transduce gustatory information to the brain via gustatory afferents. Receptors for endocrine and incretin hormones, including oxytocin (Oxt) and GLP-1, are expressed on TBCs. However, little is known about the role they play in modulating taste and food intake. We acutely and chronically delivered GLP-1 (7-36) or Oxt topical lingually in rats and assessed food intake and body weight. Acute administration of Oxt had no effect on food intake, while GLP-1 (7-36) significantly suppressed high-fat diet (HFD) intake. For chronic administration, rats were implanted with an intraoral cannula connected to a mini-pump for continuous delivery. GLP-1 (7-36) significantly suppressed HFD intake and delayed body weight gain relative to vehicle treated rats. Oxt resulted in a significant reduction in weight gain relative to vehicle treated rats. Collectively, these pilot studies reveal that the tongue may be a promising target for drug delivery in obesity, however more work is needed to fully utilize this approach.

P322

Hypothalamic Melanin-Concentrating Hormone Neurons Enhance Meal Size And Sucrose Seeking

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Melanin-concentrating hormone (MCH) is an orexigenic neuropeptide found exclusively in the lateral hypothalamic area (LHA) and zona incerta (ZI) with projection targets that span the entire brain. While multiple lines of evidence indicate a functional role for MCH in driving food-motivated and consummatory behaviors, the role of LHA vs. ZI MCH neuron populations in these processes is poorly understood. Here, to evaluate the role of LHA^{MCH} neurons (independent of ZI^{MCH} neurons) in driving appetitive responding, we injected an MCH-specific excitatory DREADD (AAV2-rMChp-hM3Dq-mCherry) into the LHA and subsequently administered either vehicle or deschloroclozapine (DCZ; DREADD ligand) during brief-access taste tests for both sucrose and maltodextrin. While LHA^{MCH} neuron activation did not change taste-guided responding, it augmented motivation to obtain carbohydrates as measured by an increase in the number

of trials initiated in the Davis rig. We next monitored chow consumption in a BioDAQ apparatus and found that chemogenetically activating LHA^{MCH} neurons via DCZ increased total chow intake during the dark/nocturnal cycle, an effect driven by an increase in meal size but not meal frequency. Finally, to assess the functional connectivity of these neurons, we chemogenetically activated the LHA^{MCH} neurons and injected radiolabeled 2-deoxy-D-glucose to measure glucose utilization as a proxy of neural activity. Results revealed bidirectional modulation of multiple brain sites, including striatal and midbrain dopaminergic structures associated with nutrient reinforcement. Taken together these results suggest that LHA^{MCH} neurons play a functional role in food-driven motivated behaviors, potentially via downstream activation of mesostriatal regions.

P324

Oxytocin Conditions Flavor Preference And Drives Accumbal Dopamine Release

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Animals learn to prefer flavors that predict the post-ingestive consequences of nutrients, but the signals that convert nutrient detection into reinforcement remain poorly understood. Prior work showed that CCK and ghrelin are not sufficient to support conditioned flavor preference, leaving unresolved whether any circulating hormone can drive flavor reinforcement. We hypothesized that a circulating hormone can engage mesolimbic dopamine and reinforce flavor preference. **Results:** To identify candidate mediators, we measured nucleus accumbens dopamine release with in vivo fiber photometry after intraperitoneal delivery of a cocktail of four hormones. The cocktail increased accumbal dopamine activity, suggesting that one or more circulating hormones may engage reward circuitry (n=10, p<0.05). We next tested each hormone individually and found that only oxytocin reproduced the dopamine response observed with the cocktail (n=10, p<0.05). Having identified oxytocin as the only hormone sufficient to evoke accumbal dopamine release, we tested whether it was also sufficient to support flavor reinforcement learning. Consistent with imaging, only oxytocin induced flavor preference (n=16, p<0.05). Finally, to test whether oxytocin-driven reinforcement requires vagal sensory signaling, we ablated vagal sensory neurons expressing oxytocin receptors and repeated the conditioning paradigm. Vagal OxtR neuron ablation blunted oxytocin-induced flavor preference (n=10, p=ns). **Conclusion:** Oxytocin is a circulating hormone sufficient to activate accumbal dopamine and drive flavor reinforcement learning. Together, this work identifies oxytocin as a humoral signal that acts through a vagal sensory pathway to transform post-ingestive nutrient information into learned food preference.

P326

Alzheimer's Disease Rat Model Shows Increased Body Weight With Reduced Sweet Reward Consumption

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Alzheimer's disease (AD) is known to have comorbidities with obesity and diabetes, with obesity during midlife being a top risk factor for developing AD. To examine the relationship between AD and weight, we conducted palatable reward consumption tests (i.e., sucrose preference, FrootLoops) and assessed locomotor activity at different age timepoints (6-7 and 10-13 months). To do this, we used the transgenic rat line TgF-344, which carries two human gene mutations (APP and PSEN-1) to recapitulate familial AD. Consistent with clinical observations, we found that AD animals weigh more compared to wild type littermates by 6 months of age ($F_{1,53}=23.7, p<0.0001$). To investigate if the difference in weights between genotypes influenced palatable reward consumption, we tested palatable reward preferences using 1) a two-bottle choice test of liquid sucrose (4 vs 12%) 1 hr/5 daily sessions, and 2) a two-choice food consumption test of free access to FrootLoops vs standard chow for 1 hr/5 daily sessions. We found: 1) AD rats consumed less of a high (12%) concentration sucrose compared to a low concentration of sucrose (4%; $F_{1,26}=8.99, p=0.006$) and less total caloric intake ($F_{1,26}=52.7, p<0.0001$), and 2) AD rats consumed less FrootLoops on average compared to their wild type counterparts ($F_{1,24}=5.961, p=0.02$). Next, we investigated if general locomotor activity could account for the difference in weights between genotypes. We first placed the rats into a home-cage like environment to test for locomotor activity for 30 minutes over 5 days. We found no difference in locomotor activity between the two groups ($t_{26}=0.03, p=0.97$). The lack of difference in locomotor activity indicates alternative mechanisms driving this increased body weight and reduction in sweet reward consumption.

P328

Adolescent Morphine Exposure Amplifies Rewarding And Withdrawal Effects On Dopamine Signaling During Adulthood Re-Exposure

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Adolescent use may cause long-term changes in reward circuitry responsiveness. Prior work in our lab used intracranial self-stimulation (ICSS) to show that pre-exposure to morphine during adolescence increased reward sensitivity during morphine administration in adulthood, but exacerbated decreases after discontinuation. We hypothesized that adolescent pre-exposure would enhance dopamine (DA) signaling to the reinforcing effects of morphine, with greater development of tolerance during adulthood administration, and that discontinuation of morphine will result in a greater suppression of DA activity compared to adolescent morphine naïve controls. Here we utilized in vivo fiber photometry (NAcLS dLight1.3b) to test the effects of adulthood morphine administration and withdrawal on DA release in rats pre-exposed to morphine during adolescence (n=11 control, n=12 adolescent morphine). During adulthood morphine administration, we found that adolescent morphine pre-exposure initially heightened increases in reward sensitivity, spontaneous DA transients, and stimulated DA release, which reduced across repeated administrations. Following morphine discontinuation, we observed suppression in reward sensitivity, spontaneous DA transients, and stimulated release. Together, adolescent morphine exposure increases both the rewarding effects of later morphine administration and the aversive effects of withdrawal, indicating that reinforcer pathology may drive increased susceptibility to maladaptive behaviors in adulthood. Further research will explore mechanisms underlying these shifts and potential interventions, including determining if the use of GLP1 agonist treatments can mitigate the effects of morphine upon re-exposure.

P330

Neurobehavioral Mechanisms Underlying The Efficacy And Tolerability Of The Amylin Analog Cagrilintide In RatsSophia L Fischer^{1,2}, Allison M Pataro^{1,2}, Serena X Gao^{1,3}, Ann Law¹, Fatma Cicek¹, Rebecca Pan¹, Claire Katen¹, Tito Borner¹¹Department of Biological Sciences, University of Southern California, Los Angeles, CA, United States, ²Integrative and Evolutionary Biology Graduate Program, University of Southern California, Los Angeles, CA, United States, ³Neuroscience Graduate Program, University of Southern California, Los Angeles, CA, United States

Recent advances in incretin-based therapies have markedly improved treatment outcomes in obesity. However, current FDA-approved incretin-based therapeutics are frequently associated with nausea and emesis, which reduce treatment adherence and limit the use of higher doses. There is therefore a critical need for alternative strategies that can achieve comparable metabolic efficacy while improving tolerability and long-term compliance. The pancreatic hormone amylin promotes satiation with minimal aversive effects, positioning amylin analogs as promising anti-obesity agents. Cagrilintide, a long-acting amylin analog, has demonstrated robust weight reducing effects in clinical trials. However, the neurobehavioral mechanisms underlying its efficacy and tolerability remain poorly understood. Here, we combine behavioral, pharmacological and surgical approaches to show that cagrilintide dose-dependently suppresses food intake and body weight in rats, while eliciting only minimal indices of malaise. Furthermore, central administration demonstrates that the hindbrain is sufficient to mediate the hypophagic and body weight lowering effects of cagrilintide, whereas complementary lesion studies identify the area postrema of the hindbrain as a critical site required for these actions. Together, these findings identify a hindbrain-mediated mechanism underlying cagrilintide's efficacy and support its favorable tolerability profile, positioning amylin-based therapies as promising complementary or alternative approaches to incretin-based obesity treatments.

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From Ads To Appetite: Food Commercials Increase Reward-Related Brain Activation To High Energy-Dense FoodsKyle Hallisky¹, Bari Fuchs¹, Alaina L Pearce¹, Mya A Knappenberger¹, Stephen J Wilson¹, Travis Masterson¹, Emma J Rose¹, Frank G Hillary¹, Amanda Bruce², Seung-Lark Lim³, Kathleen L Keller¹¹The Pennsylvania State University, University Park, PA, United States, ²University of Kansas Medical Center, Kansas City, KS, United States, ³The University of Alabama, Tuscaloosa, AL, United States

Food advertising is a potent environmental cue believed to increase craving and appetitive motivation by activating dopaminergic reward circuitry. This may pose a threat to children with significant media use, particularly if it alters food cue reactivity beyond length of the advertisement. We tested whether exposure to rewarding commercials (fast food vs gender-neutral toys) differentially altered brain responses to subsequent food images. Eighty-seven 7-9-year-old children (52% female) without obesity (BMI%<90) completed functional magnetic resonance imaging (fMRI) at baseline of a yr-long longitudinal study. During fMRI, children viewed food and toy commercials followed by images of high (HED>1.5 kcal/g) and low (LED<1.5 kcal/g) energy-dense foods. Whole brain analyses tested activation to (1) food vs toy ads, (2) HED images after food vs toy ads, and (3) LED images after food vs toy ads. One-sample *t*-tests on subject-level contrasts controlled for motion, sex, pre-MRI fullness, and anxiety. Results were voxel-wise thresholded at $p<.001$ with cluster corrected $\alpha=.05$. There was greater activation during food ads vs toy ads in gustatory, salience, and decision-making regions (i.e., insula/frontal operculum, anterior cingulate, and orbitofrontal cortex). Following food vs toy ads, there was greater activation for HED food images in reward/motivation (bilateral caudate, putamen), gustatory (insula/frontal operculum), motor (precentral gyrus) and attentional control (dorsolateral prefrontal cortex) regions. No differences were seen for LED foods. Greater striatal reward circuitry engagement to palatable, high energy-dense foods after fast food commercials may reflect a neural mechanism by which food marketing influences children's eating behavior and obesity risk.

P334

A Cerebellar Node For Gut-Derived Satiety SignalingA-Hyun Jung¹, Aloysius Y.T. Low¹, Dillon Nittoli¹, Albert T.M. Yeung¹, Brook Weller¹, Emily Song¹, Amber Alhadeff^{2,3}, J. Nicholas Betley^{1,3}¹Department of Biology, University of Pennsylvania, Philadelphia, PA, United States, ²Monell Chemical Senses Center, Philadelphia, PA, United States,³Department of Neuroscience, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States

Cerebellar output neurons have recently emerged as regulators of food intake, but the meal-related signals that recruit these neurons and the broader feeding circuits they engage remain unclear. To define the function and characteristics of cerebellar neurons activated during a meal, we used Fos2A-iCreER mice to express chemogenetic actuators or calcium indicators in lateral deep cerebellar nucleus (latDCN) neurons activated during high-fat diet refeeding. Chemogenetic activation of meal-activated latDCN neurons significantly reduced food intake without affecting energy expenditure or motor performance, indicating a selective role in feeding regulation. Fiber photometry calcium imaging revealed that meal-activated latDCN neurons were robustly activated by intraperitoneal administration of the gut-derived satiety hormone cholecystokinin (CCK), but not by sensory food cues, active food consumption, or visceral inflammatory signals, demonstrating selective sensitivity to physiological satiety signals rather than generalized visceral discomfort. Pretreatment with the CCK1 receptor antagonist Devazepide attenuated CCK-evoked calcium responses, supporting a CCK1R-mediated mechanism for recruitment of this cerebellar population. In contrast, GLP1 and the GLP1 receptor agonist Exendin-4 failed to elicit calcium responses. Whole-brain cFos activation patterns following stimulation of meal-

activated DCN versus NTS neurons further suggest that cerebellar satiety signaling may engage pathways separable from canonical GLP1- and NTS-mediated anorexigenic circuits. Together, these findings identify the latDCN as a previously unrecognized central node for gut-derived satiety signaling and reveal its contribution to the broader neural architecture of gut-brain communication.

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Beta Glucan Supplementation Reduces Meal Size And Preserves Glp-1 Agonist Response On A High-Fat Diet

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Soluble fiber supplementation reduces energy intake and body weight gain in rodents on high-fat (HF) diets, possibly through enhanced satiation or satiety signaling, but detailed behavioral mechanisms are unclear. We examined meal patterns through the transition to HF diet with and without soluble fiber in the form of beta glucan (BG), and asked whether BG supplementation would preserve sensitivity to low dose GLP-1 agonist treatment. Adult male rats were housed in the BioDAQ continuous food intake monitoring system and switched from chow to a 45% fat diet with either 7% cellulose (HF-C; n=9) or 10% BG (HF-BG; n=9). Linear Mixed Models assessed intake and meal patterns over 4 weeks. Both groups increased kcal intake upon HF diet introduction, but HF-BG rats returned to chow baseline by week 3, while HF-C intake remained elevated at that point. HF-BG rats significantly (p 's <0.05) reduced dark-phase meal size at week 1 and took smaller meals than HF-C rats at weeks 1 and 3, with a transient compensatory increase in meal number at week 1. Body weight gain did not differ significantly between groups. After 3 weeks on diet, rats received IP vehicle or Ex4 (0.1 μ g/kg) 30 min before dark onset in a within-subjects, counterbalanced design. For Ex4 response, there were significant (p 's <0.05) effects of diet, drug, and time on intake across hours 1-12 of the dark phase. We previously showed that HF diet impairs Ex4 response in rats, and replicated this in the present HF-C group. Ex4 suppressed intake in HF-BG rats (p <0.05), with no significant effect in HF-C rats. These findings indicate that BG supplementation attenuates HF hyperphagia primarily by reducing meal size and preserves GLP-1 response that is otherwise impaired by HF diet, warranting further investigation.

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Differential Gut-Brain Signaling Mechanisms For Fructose And Glucose

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Our modern diets contain high levels of added sugars, especially glucose and fructose. While these sugars share a chemical formula and caloric content, accumulating evidence indicates they have distinct effects on metabolism and behavior. Here, we examined the gut-brain mechanisms by which glucose and fructose are sensed to influence neural activity in calorie-responsive hypothalamic agouti-related protein (AgRP) neurons. Monitoring AgRP neuron activity via fiber photometry, we found that fructose was less effective than glucose at inhibiting AgRP neuron activity (n=10, two-way ANOVA p <0.05), a finding that challenges the model of AgRP neurons as indiscriminate calorie detectors. To determine the functional relevance of the attenuated AgRP neuron response to fructose, we trained mice to lick for flavors associated with AgRP neuron inhibition that mimicked the response to fructose or glucose. Mice developed a strong conditioned preference for a flavor paired with the larger AgRP neuron inhibition that mimicked glucose over a flavor that mimicked fructose, suggesting that the blunted neural response to fructose is instructive for food preference (n=10-12/group, two-way ANOVA, p <0.01). We next measured levels of satiation hormones and found that intragastric fructose evokes higher levels of plasma peptide YY (PYY) compared to glucose (n=11-13/group, one-way ANOVA p <0.0001). Given that PYY can act on Y2R on vagal afferent neurons, we performed *in vivo* imaging of Y2R-expressing vagal neurons and found distinct subpopulations that are activated by either fructose (n=69) or glucose, (n=56) and some neurons responding to both (n=41). Further, ablation of Y2R-expressing vagal neurons only abolished fructose- but not glucose-induced inhibition of AgRP neuron activity (n=4/group, unpaired t-test p <0.05). Therefore, fructose engages a Y2R-expressing vagal-to-hypothalamic pathway and is less effective than glucose at inhibiting activity in AgRP neurons, effects that have functional consequences for food choice.

P340

Hindbrain Glp-1R Signaling Reduces Instrumental Responding For Food And Drugs

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Glucagon-like peptide-1 receptor (GLP-1R) agonists like semaglutide have been effective in reducing food intake and promoting weight loss by reducing motivation to eat. Recent evidence suggests these medications may also reduce motivation for many commonly abused drugs. Here we show semaglutide (60 μ g/kg; s.c.) reduces instrumental responding for sucrose (paired t-test; n=8, p <0.001) and self-administered i.v. cocaine (0.5 mg/kg/infusion; n=7, p <0.01) in male and female mice. Using fiber photometry monitoring of the GRAB-DA2h sensor, we observed systemic semaglutide was associated with reduced nucleus accumbens DA signaling to food (n=13, p <0.05) and cocaine (n=4, p <0.05). We uncover the hindbrain dorsal vagal complex (DVC) as a key regulator of this reduction in motivation. We show chemogenetic activation of DVC^{GLP-1R} neurons reduces operant responding for sucrose (paired t-test; n=14, p <0.001) and i.v. cocaine (0.5 mg/kg/infusion; n=9, p <0.001), phenocopying the effects of semaglutide. The effects of semaglutide (n=11) and DVC^{GLP-1R} neuron activation (n=12) on instrumental responding are due to changes in motivation to work for reward rather than nonspecific motor effects. We tested mice on the rotarod (1-Way ANOVA; CNO p =ns; semaglutide p =ns), forced swim test (2-way ANOVA; CNO p =ns; semaglutide p =ns), hot plate test (paired t-test; CNO p =ns; semaglutide p =ns), and baseline locomotion (paired t-test; CNO p =ns; semaglutide p =ns), and found neither semaglutide nor DVC^{GLP-1R} neuron activation

significantly affected these parameters. Overall, our results suggest semaglutide and DVC^{GLP-1R} neurons in the hindbrain influence incentive motivation and dopamine signaling, offering insight into how GLP-1-based therapeutics curb both food- and drug-motivated behaviors.

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Differences In Basal And Diet-Induced Changes In Nucleus Accumbens Inhibitory Transmission In Obesity-Prone And Obesity-Resistant Rats.

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Obesity is a global public health issue, partly driven by overconsumption of calorie-dense, palatable foods. Activity of the Nucleus Accumbens (NAc) plays a key role in eating and its function is altered by the consumption of a “junk-food” diet (JF). For example, we found that JF diet consumption enhances NAc excitatory transmission and responsivity to excitatory drive in obesity-prone (OP), but not in obesity-resistant (OR) rats. However, no studies have examined effects of obesogenic foods on NAc inhibitory transmission. Furthermore, the endogenous opioid system plays a crucial role in food intake, and prior work suggests that NAc endogenous opioid systems differ in OPs vs ORs. Therefore, here, adult male OP and OR rats were given access to JF or chow diet. Then, whole-cell patch clamping recordings were used to measure the effects of JF on frequency, amplitude, cumulative frequency, and paired-pulse ratio (PPR) of inhibitory activity (sIPSC) and the effect of opioid receptor agonists and antagonists on inhibitory transmission. Preliminary results show that JF decreases inhibitory activity in OP but not OR rats. In contrast, JF diet had no effects in ORs, but basal inhibitory activity was lower in ORs compared to OPs. In addition, in OPs the opioid receptor antagonist naloxone (10 μ M) produced larger reductions in sIPSC frequency in JF vs chow groups; this effect was absent in ORs. These findings suggest that JF reduces inhibition in the NAc the regulation of inhibition by opioids in ways that may promote eating.

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Early-Life Diet Primes Long-Term Responsivity To Glucagon-Like Peptide 1 Receptor Agonists (Glp1Ras) In Rats

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GLP1RAs are effective treatments for type 2 diabetes and obesity, improving glucose homeostasis and promoting weight loss through coordinated effects on food intake and metabolism. However, up to 30% of patients fail to respond, showing limited weight loss or glycemic improvement after sustained treatment. Environmental factors, including perinatal nutrition, may contribute to this variability by programming long-term metabolic and behavioral outcomes. This study tested the hypothesis that perinatal exposure of rats to a maternally consumed obesogenic diet alters adult responsivity to the GLP1RA exenatide (Ex4). Dams were maintained on either standard chow or chow plus a high-fat, high-sugar Western diet (WD) throughout lactation and gestation. All offspring were weaned onto chow at postnatal day (P)21 and maintained on chow until early adulthood (P60), at which point WD-reared (WDR) rats exhibit typical BW and adiposity. Following a 6-week WD feeding challenge, WDR rats gained more fat mass and displayed persistent disruption in GLP1R-mediated signaling. Meal pattern analysis revealed that WDR rats exhibit reduced latency to initiate eating and consume larger first meals compared to chow-reared (CR) rats when exposed to WD. Notably, these effects were restricted to the early dark phase, with no differences in 24-hour intake. In response to Ex4 (1, 3, 10, 25 μ g/kg), both male and female WDR rats exhibited attenuated BW loss, while only WDR male offspring experienced blunted Ex4-induced hypophagia. Together with additional evidence that WD rearing reduces Ex4-induced hypothermia, these findings suggest that both behavioral and metabolic mechanisms contribute to blunted GLP1RA responsivity.

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The Effects Of A High-Fat, High-Sugar Diet On Delay Discounting And Sensitivity To Haloperidol In Male And Female Rats Exposed During Adolescence Vs. Adulthood

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Delay discounting (DD) is a psychological process by which delayed outcomes are associated with lower reinforcing effects relative to immediate outcomes. Previous work suggests chronic consumption of a high-fat, high-sugar diet (HFHS) increases DD and sensitivity to haloperidol (dopamine antagonist), suggesting changes in dopamine receptors. In the current study, we examined the extent to which a chronic HFHS diet altered DD and sensitivity to haloperidol in male and female Long-Evans rats exposed at 21 or 70 days old ($n = 8$ /group). We exposed rats to a 60-day diet exposure during which rats were fed an unlimited amount of a HFHS diet or standard rat chow (control) diet. Rats completed a DD task in which responding on one side resulted in a grain-based food pellet delivered immediately (SS) vs. three food pellets delivered after a delay (LL). Delays started at 0, 1, 2, 4, and 8-s and increased (by 2x and 4x each for delay) between

sessions until each rat chose the delayed alternative 50% of the time or less. After stable choice, weekly injections of haloperidol (0, 0.03, 0.1, and 0.3 mg/kg) commenced. All rats decreased LL choice as delay increased ($p < 0.001$) and made fewer LL choices as dose of haloperidol increased ($p < 0.001$) regardless of diet. For female rats, LL choice depended on the delay, diet, age at diet exposure, and dose of haloperidol ($p = 0.04$). Previous work suggest HFHS diet alters DD; however, the current study included a different DD procedure, strain of rats, diet ingredients, and did not screen for weight gain prior to behavioral testing. Ongoing work will continue investigate the conditions under which exposure to a HFHS diet alters DD, as DD may contribute to overconsumption of HFHS foods.

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Control Of Consummatory Behavior By Lateral Hypothalamic D1R Neurons Projecting To The Anterior Thalamus

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The lateral hypothalamus (LH) regulates feeding and consummatory behaviors, yet the circuit mechanisms through which specific LH neuronal populations control these behaviors remain poorly understood. LH Dopamine D1 receptor-expressing (D1R) neurons are implicated in feeding regulation, as pharmacological manipulation of LH dopaminergic signaling suppresses food intake. However, the function, underlying activity dynamics, and downstream circuitry of LH D1R neurons are unclear. We hypothesized that LHA D1R neurons are critical regulators of feeding behavior by modulating consummatory actions. To test this, we combined two-photon calcium imaging, optogenetic manipulations, and circuit tracing in D1-Cre mice. Optogenetic LH D1R neuron stimulation suppressed food intake and induced place aversion (ChR2, n=6; YFP, n=6). To assess stimulation effects on consummatory microstructure, we performed a head-fixed licking task. LH D1R neuron stimulation robustly increased licking, suggesting that feeding suppression is caused by aberrant consummatory behavior without driving hunger or food approach. Two-photon calcium imaging revealed that LH D1R neuronal activity is tightly correlated with licking and persists in the absence of reward, suggesting these neurons encode consummatory motor actions rather than reward value (n=6). Anterograde tracing revealed a prominent projection to the Interanterodorsal Thalamus (IAD). LH D1R→IAD stimulation recapitulated the effects observed with cell-body stimulation, promoting licking while suppressing feeding and producing place aversion (ChR2, n=10; YFP, n=6). These findings identify an LH D1R→IAD circuit that modulates consummatory motor output and highlight a dissociation between the neural control of consummatory actions and feeding motivation.

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High-Fat Diet Disrupts Circadian Eating Via Microbiota&Ndash;Vagal Signaling

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Eating is normally aligned with circadian state, and mistimed eating contributes to obesity. In mice, high-fat diet (HFD) increases intake during the inactive light phase without increasing dark-phase intake, and restricting HFD access to the dark phase prevents obesity. Because HFD disrupts gut microbial rhythms, we hypothesized that rhythmic microbiota-derived signals control eating via gut-brain pathways and that HFD disrupts this circadian signaling. **Methods:** Sterile-filtered fecal supernatants were collected from chow diet- and HFD-fed mice during the first hour of the light (ZT1) and dark (ZT13) phases. Feeding responses were measured after supernatant administration, and in vivo two-photon calcium imaging was used to assess vagal sensory neuron responses in the nodose ganglia. **Results:** HFD increased light-phase eating within the first week of exposure, and this altered rhythm persisted for at least 7 weeks. In chow-fed mice, ZT1 supernatants suppressed food intake relative to ZT13 supernatants, demonstrating a time-of-day-dependent microbial effect on feeding. This effect was lost in HFD-fed mice, indicating that HFD disrupts rhythmic microbial signals that normally restrain inappropriate light-phase intake. Calcium imaging showed that colonic supernatants activate vagal sensory neurons, with distinct response patterns to light- versus dark-phase samples, indicating that vagal sensory neurons discriminate circadian microbial signals. **Conclusion:** These data identify a microbiota-vagal pathway that encodes circadian information and is altered by HFD. Disruption of this pathway by HFD may promote inappropriate light-phase feeding and promote obesity.

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Gut Vagal Sensing Links Ethanol Ingestion To Reward And Binge Drinking

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Alcohol shares key features with food. It contains calories, is orally ingested, and is highly palatable. Consistent with a role for gut brain signaling, vagotomy reduces alcohol intake, suggesting that peripheral sensory pathways contribute to alcohol consumption. We therefore hypothesized that ethanol is detected in the gut by vagal sensory neurons that drive reward and motivation. Using in vivo calcium imaging and FosTRAP labeling in female mice, we identified a subset of nodose ganglion neurons that respond selectively to intragastric ethanol. These neurons exhibit rapid, time locked responses and are consistently reactivated, consistent with receptor mediated detection. To test function, we used FosTRAP mice combined with viral delivery of caspase or DREADD constructs to selectively ablate or activate ethanol responsive vagal neurons in the nodose ganglia. These neurons were both necessary and sufficient for alcohol directed behavior. Ethanol in the gut increased nucleus accumbens activity, measured by cFos and dopamine photometry, and this response was abolished by ablation of ethanol responsive vagal neurons. Loss of this population reduced motivation to obtain alcohol and prevented escalation to binge like drinking in the dark paradigm. Together, these findings define a gut brain circuit linking ethanol sensing to dopamine dependent reward, motivation, and binge drinking. Importantly, the selective reduction in binge like intake suggests that targeting this pathway may represent a therapeutic strategy for alcohol use disorder.

P354

Semaglutide-Associated Restructuring Of The Gut Microbiome In Rats.Suyeun Byun¹, Morgan R Sotzen², Mya A Knappenberger¹, Madison T Bento², Mohammed Asker³, Karolina P Skibicka²¹Pennsylvania State University, State College, PA, United States, ²University of Calgary, Calgary, AB, Canada, ³University of Gothenburg, Gothenburg, Sweden

Semaglutide (SEMA), a glucagon-like peptide-1 receptor agonist, produces robust weight loss by reducing food intake, yet its effects on the gut microbiome remain incompletely understood. We hypothesized that SEMA reshapes gut microbial composition and that these shifts are associated with metabolic outcomes. Male and female SD rats (n=10–12/group) were assigned to control, pair-fed (PF), or SEMA-treated groups. Body weight and food intake were measured during the 4-week treatment. Gut microbial composition was analyzed using 16S rRNA sequencing. SEMA significantly reduced body weight gain and food intake in both sexes. SEMA increased microbial richness but reduced evenness, while Shannon diversity was unchanged. Beta diversity analyses revealed significant differences among groups. LEfSe identified enrichment of Firmicutes taxa, particularly Clostridiaceae, in SEMA-treated rats, whereas controls showed greater representation of Bacteroidota. Many changes reflected a potentially deleterious microbial profile (e.g., 500x increase in *Clostridium perfringens*, 70% reduction in Bacteroides, loss of Lachnospiraceae ASF356). Correlation analyses revealed negative correlations between Firmicutes abundance and body weight change and positive correlations between Bacteroidota abundance and body weight change in males. In females, fewer associations were observed, although Bacteroidota remained positively correlated with body weight change. Together, these findings demonstrate profound, and not necessarily health positive, gut microbial community shifts occur following GLP-1 analogue treatment, with many of the changes in the gut microbiota not simply due to the decreased food intake and weight loss resulting from the drug.

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Involvement Of The Nucleus Accumbens And The Paraventricular Nucleus Of Thalamus In The Estrogen-Induced Enhancement Of Sweet Taste Preference In RatsNatsumi Kosugi¹, Mana Uchida¹, Fuka Nishino¹, Keiko Morimoto^{1,2}, Akira Takamata¹¹Nara Women's University, Nara, Japan, ²Kyoto Koka Women's University, Kyoto, Japan

Estrogens, primarily estradiol, are well established to exert anorectic and anti-obesity effects via the homeostatic feeding regulation. However, estrogen's role in hedonic feeding regulation, especially in sweet taste preference, remains to be elucidated. To address this issue, we examined the intake of 10% (w/v) sucrose solution, water, standard rodent diet, and total energy (the sum of energy from sucrose and diet) in ovariectomized rats with or without estradiol replacement (E2(–), E2(+)) and in sham-operated rats. Both serum estradiol levels and sucrose preference (defined as the percentage of energy derived from sucrose solution relative to total energy intake) were highest in the E2(+) group, intermediate in the sham group, and lowest in the E2(–) group. These results suggest that estrogens enhance sucrose preference in an estrogen level-dependent manner. To further investigate the underlying neural mechanisms, we evaluated neural activation in the nucleus accumbens (NAc), a key region of the brain reward system. Retrograde tracing using cholera toxin subunit B (CTB) injected into the NAc revealed direct neural projections from the paraventricular nucleus of the thalamus (PVT). In the E2(+) group, ΔFosB expression in the NAc was higher in rats consuming sucrose than in those consuming water. Furthermore, sucrose intake altered the correlation of chronic neural activity between the PVT and NAc only in the E2(+) group. Taken together with previous findings, the functional connectivity of neural activity between the PVT and NAc may contribute to estrogen-induced enhancement of sucrose preference.

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Nmur2-Selective Agonists Provide A Well-Tolerated Therapeutic Opportunity For ObesityVolker Mack¹, Bekir Altas¹, Emmanuelle Balme¹, Katherin Bleymehl¹, Giuseppe Bruschetta², Jonas Doerr¹, Bettina Gerner¹, Daniel Lam¹, Damian Matera², Felix Schiele¹, Aaron Teitelbaum², Holger Wagner¹, Tina Zimmermann¹, Anton Pekcec¹¹Boehringer Ingelheim Pharma GmbH & Co.KG, Biberach, Germany, ²Boehringer Ingelheim Pharma GmbH & Co.KG, Ridgefield, CT, United States

Obesity remains a major health challenge and a leading cause of metabolic diseases. Effective treatments such as advanced GLP-1 receptor (GLP-1R) agonists have transformed the therapeutic landscape, yet their use can be associated with gastrointestinal (GI) side effects and requires dose-escalation regimens. This motivates exploration of complementary mechanisms that improve patient experience and broaden therapeutic options. NeuromedinU receptor 2 (NMUR2), a central Gq-coupled GPCR, has emerged as compelling anti-obesity target. Genetic and pharmacological studies have shown that NMUR2 regulates feeding behavior and energy balance. We developed potent and selective NMUR2 peptide agonists with the potential for once-monthly administration through sequence engineering and targeted lipidation, enabling reduced renal clearance and prolonged half-life. These agonists robustly suppressed food intake and induced dose-dependent body weight loss in diet induced obese mice, driven by reduction in fat mass while sparing lean mass. C-Fos immunohistochemistry and calcium imaging in hypothalamic slices confirmed engagement of arcuate nucleus pathways, supporting the mechanistic concept of enhanced satiety. The central expression profile of NMUR2 and behavioral data indicated minimal aversive or emetic liability, and experimental studies confirmed favorable GI tolerability in rodents and higher species. Co-administration with a GLP-1R agonist produced additive effects on food intake and weight loss, demonstrating mechanistic complementarity. Our data establish NMUR2 agonists as promising anti-obesity agents offering competitive weight loss; superior GI tolerability without up-titration; potential for once monthly administration; and a foundation for tolerable combinations beyond GLP-1.

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Energy State-Dependent Regulation Of Glucagon-Like Peptide 1-Releasing Neurons In The Nucleus Of The Solitary Tract

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Over one-third of the U.S. is affected by obesity, a major risk factor for cardiovascular disease, type II diabetes, hypertension, and psychiatric disorders. The FDA has approved several drugs that reduce appetite and bodyweight by targeting glucagon-like peptide-1 receptors (GLP-1Rs). Several preclinical/clinical studies have showed that activation of GLP-1Rs in the brain lowers food intake and induces weight loss; however, the effects of energy status on the endogenous GLP-1 system in the brain remain unclear. In this study, we measured the impact of energy status on the neurophysiology of preproglucagon-expressing neurons (Gcg) in the nucleus tractus solitarius (NTS). We divided adult Gcg-GFP mice (>8 weeks old) into three groups of distinct energy states: 24-hour food deprivation, 1-hour refeeding following 24-hour food deprivation, and ad libitum feeding. We used slice electrophysiology to assess neuronal excitability and neuronal firing across energy states and between sexes. Using loose-patch recordings, we saw a significant decrease in GcgNTS neuron firing rate in food-deprived male mice. In whole-cell mode, we found that 24-hour food deprivation significantly reduced the excitability of GcgNTS neurons, an effect that rescued by refeeding. Additionally, Fos immunolabeling experiments showed that GcgNTS neurons are significantly activated after intermittent access to palatable food and the magnitude of Fos activation was linearly correlated with food intake in mice given ad libitum intermittent access to palatable food. These data demonstrate sex-dependent plasticity in the activity of the brain's GLP-1-producing system. In future studies, we will investigate possible differences in synaptic transmission in GcgNTS neurons across energy states.

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Weight Loss Surgeries Divergently Regulate Alcohol Intake: Roles Of Ghrelin And The Vagus Nerve

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Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) are effective long-term weight-loss therapies. Interestingly, both human and rodent studies report marked changes in alcohol intake after these procedures: RYGB increases intake of low-concentration alcohol, while SG suppresses alcohol intake across concentrations. These studies tested the hypothesis that anatomical differences between procedures drive these opposing effects. Specifically, severing the gastric branch of the vagus nerve and retaining an empty gastric remnant promotes alcohol intake, whereas removal of the gastric body, and the ghrelin it produces, suppresses intake. Understanding this interaction is important because a meaningful subset of patients transition from SG to RYGB for additional weight control. Across three studies, 6–10 Sprague-Dawley rats per group were randomized to surgical manipulations isolating these anatomical factors. Study 1 compared anterior gastric branch vagotomy with sham surgery. Study 2 compared sham, RYGB, SG, and RYGB with removal of the gastric remnant. Study 3 compared sham, SG, and SG with anterior gastric vagotomy. Body weight, food intake, and voluntary ethanol consumption were monitored. ANOVA revealed robust surgical effects on ethanol intake: vagotomy increased intake, whereas gastrectomy suppressed intake. Post-hoc comparisons showed that removal of the gastric remnant or gastric fundus (as in SG) strongly suppressed ethanol intake, even in the presence of gastric branch vagotomy. These findings support the continued rise in SG over RYGB, particularly for individuals at risk of alcohol use disorder. Importantly, they also suggest that SG may confer lasting protection against increased alcohol intake even if patients later transition to RYGB.

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Macronutrient-Specific Responses To Protein Restriction Are Linked To Peripheral Taste Signaling

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Protein restriction drives a macronutrient intake shift toward protein over carbohydrate, termed protein appetite. While the T1R1+T1R3 receptor mediates oral protein detection ('umami'), the taste system's contribution to protein appetite remains unclear. We leveraged mouse strains differing in T1R3 sensitivity: sensitive C57BL/6J (B6) and subsensitive 129/J (129). Adult males (~20 weeks) were maintained on a normal (20%, NP) or low-protein diet (5%, LP) for 9 days. Preference was assessed via two-bottle choice tests (4% casein vs. 4% maltodextrin). Both strains preferred maltodextrin on NP. Under LP, B6 mice selectively increased casein intake without altering carbohydrate intake, reflecting an active protein-seeking response. Conversely, 129 mice decreased maltodextrin intake without increasing casein, indicating suppressed carbohydrate drive. We quantified expression of taste receptors (Tas1r1, Tas1r3) and metabolic enzymes (Gck, Mgam) in circumvallate papillae. On NP, 129 mice showed higher Tas1r1 expression than the LP group. LP upregulated Tas1r1 in B6, paralleling increased protein intake, but not in 129 mice. Instead, LP suppressed Tas1r3 and Gck in 129 mice. As Tas1r3 and Gck involve sugar sensing, these results align with reduced carbohydrate intake in this subsensitive strain. In summary, both strains responded to protein restriction through distinct strategies (increased protein intake vs. decreased carbohydrate intake), explaining individual variability in responses and highlighting peripheral taste signaling as a key contributor to these nutrient-specific behaviors.

2:00 - 3:00 PM	Regency Foyer
Coffee Break & Exhibits	
3:00 - 4:30 PM	Regency B
Symposium 3: Gut Check: Mechanosensory signals in satiation	

Chair(s): Claire de la Serre
3:00

Dietary Substitute Sugars&Rsquo; Osmotic Signaling Engages An Ileal Brake To Control Gut Motility And Feeding Via Glp-1

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Modern diets are replete with poorly absorbed sugar substitutes like sugar alcohols (e.g., xylitol) that impose unusually high luminal osmolar loads, yet how the gut senses these non-nutritive osmoles to regulate ingestion is unclear. Here, we show that luminal hyperosmolarity triggers an ileal brake–like response that slows proximal gut transit and suppresses feeding via gut hormone release. In mice, acute gavage of xylitol (vs. iso-osmotic control) caused luminal contents to accumulate in the small intestine while less reached the cecum within ~45 min, indicating region-specific slowing of ileal transit. This occurred alongside a local spike in ileal luminal osmolality (while stomach and colonic contents remained near isotonic), a ~2-fold surge in plasma GLP-1, increased gastric volume (gastric accommodation), and ~60% reduction in short-term food intake, which are all hallmarks of an ileal brake response. We focused on ileal sensing mechanisms and GLP-1–secreting enteroendocrine cells (EECs), which are known coordinators of the ileal brake, as candidate osmosensors. Mechanistic studies showed that hyperosmolar conditions directly excite EECs: patch-clamp recordings from a human L-cell model (QGP-1) revealed a dramatic ~40 mV depolarization and evoked action potentials under hyperosmotic (400 mOsm/kg) vs. iso-osmotic conditions. Similarly, ileal, but not colonic, primary EECs exhibited robust Ca²⁺ influx to hyperosmolar stimuli ex vivo, and hyperosmotic exposure of ileal organoids triggered a 2–3-fold increase in GLP-1 secretion. These findings identify an ileal epithelial osmosensory pathway that couples luminal hyperosmotic stimuli to L-cell hormone release and gut-brain-gut feedback. By engaging this pathway, non-nutritive osmoles can powerfully modulate GI motility and satiety signals, revealing a mechanistic link between acute exposure to dietary osmolarity and ingestive behavior. Together, these findings reveal dietary osmolarity as a powerful, previously underappreciated signal through which the gut translates modern food composition into hormonal control of motility, satiety, and ingestive behavior.

3:30

The Role Of Gastrointestinal Mechanosensation In Regulating

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The stomach distends to accommodate food, and the gastrointestinal (GI) tract is in constant motion as the ingested food is propelled forward. Mechanical cues from the gastrointestinal (GI) tract play an essential role in informing the brain of feeding states and regulating energy homeostasis, yet it is not well studied. While chemosensory signals, such as leptin and ghrelin, are well known, how mechanical signals induced by stomach distention contribute to energy homeostasis remains poorly defined. PIEZO1 and PIEZO2 are mechanosensory ion channels which are expressed in different organs throughout the body, including neurons that innervate the gastrointestinal tract. They open in response to mechanical force and relay mechanosensory signals via the peripheral nervous system, and are excellent candidates for the sensors that detect mechanical signals to control food intake. Previous work identified oxytocin-receptor-expressing (Oxtr+) sensory neurons as key mechanosensors that detect stretch and relay the sense of satiety to the brain. We are using Oxtr-Cre animals in combination with other genetic tools to delete PIEZO ion channels from subsets of sensory neurons and delineate how these ion channels function to modulate food intake. We found that loss of Piezo2 in Oxtr+ neurons, as well as more broadly in the sensory nervous system, altered feeding patterns despite normal body composition. We further examined hypothalamic neurons in the arcuate to determine how central feeding circuitry was engaged in the absence of mechanosensory signaling. By revealing a mechanosensory pathways parallel to established chemosensory systems, these findings open avenues for developing next-generation anti-obesity therapeutics that tap into mechanical signaling besides targeting the chemical pathways which, despite their efficacy, carry significant gastrointestinal and systemic side effects.

4:00

Pharyngeal Mechanosensation Drives Rapid Thirst Satiation

Sung-Yon Kim

Seoul National University, Seoul, South Korea

Drinking rapidly quenches thirst within seconds, a critical pre-systemic feedback that occurs well before absorbed water restores systemic balance. However, the sensory origin and neural mechanism underlying this rapid thirst satiation have remained elusive. Here, we dissociated tightly coupled processes of drinking to reveal that pharyngeal mechanosensation during the swallowing reflexes is the source of this rapid thirst satiation. This signal primarily depends on PIEZO2 in the nodose-jugular-petrosal ganglia and ascends through a pathway linking the nucleus of the solitary tract, parabrachial nucleus, and median preoptic area, ultimately inhibiting subfornical organ thirst neurons. Computational modeling and experiments reveal that this circuit operates as a high-pass filter, selectively transmitting swallowing-evoked signals only when they occur in rapid succession, a characteristic of drinking. Our findings pinpoint the long-sought sensory origin of rapid thirst satiation and delineate the pharynx-to-forebrain circuit that transforms swallowing signal into drinking-specific inhibition to quench thirst.

3:00 - 4:30 PM

Millennium Hall

Oral Session 7: Pour Some Sugar on Me: Carbohydrates & Sugar

Chair(s): Carolina Cawthon

3:00

High-Fat Diet Exposure Alters Sucrose Consumption Behaviors And Dopamine Signaling In The Nucleus AccumbensClaire M. Corbett¹, Leighelle Adrian¹, Brianna E. Linneman^{1,2}, Samantha L. Bozarth^{1,2}, Mark Niedringhaus^{1,2}, Elizabeth A. West^{1,2}¹Rowan-Virtua University School of Osteopathic Medicine, Stratford, NJ, United States, ²Rowan-Virtua School of Translational Biomedical Engineering and Sciences, Stratford, NJ, United States

With increased consumption of diets high in fat in modern societies, it is critical to consider the effects of diet on behavior and brain function. Here, we examined how a history of a high-fat diet alters reward processing, associative learning, and NAc dopamine dynamics in male and female Long-Evans rats. Rats were separated into (n=15-16/group) 1) a control group fed a standard chow diet, 2) a group fed a high-fat diet, or 3) a group fed a low-fat/high-sugar diet for 12 weeks. At week 10, we found that the high-fat diet led to a significant decrease in preference for a high concentration of sucrose (12%) vs low concentration sucrose (4%) after 7 daily sessions. Next, all rats underwent stereotaxic surgery to inject the genetically encoded GPCR-activation-based-DA (GRABDA) and optical ferrules into the NAc and were switched to a standard chow diet. Rats underwent 15 days of Pavlovian conditioning where one cue predicted a sucrose pellet (CS+) and a different cue did not (CS-) to evaluate associative learning. We measured NAc dopamine dynamics on Day 1 and 15 of Pavlovian conditioning using fiber photometry. On Day 15, all groups discriminated between CS+ vs CS- as shown by increased time spent in the food cup (diet, cue type: p<0.0001) and increased entries into the food cup during the CS+ vs CS- (diet: p=0.02, cue type: p<0.0001), indicating preservation of learning mechanisms. Rats fed the high-fat spent less time in the food cup during both cues compared to standard chow rats, suggesting diminished motivated behavior. On Day 15, high-fat rats show abolished NAc dopamine dynamics to a reward-predictive cue compared to standard chow and low-fat/high-sugar rats. Taken together, a high-fat diet alters reward processing, motivated behavior, and NAc dopamine signaling.

3:15

Amygdala&Ndash;Liver Signaling Orchestrates Glycemic Responses To StressJamie RE Carty¹, Kavya Devarakonda¹, Richard M Connor², Sarah A Stanley¹¹Diabetes, Obesity and Metabolism Institute, Icahn School of Medicine at Mount Sinai, New York, NY, United States, ²Nash Family Department of Neuroscience and Friedman Brain Institute, Icahn School of Medicine at Mount Sinai, New York, NY, United States

Behavioural adaptations to environmental threats are crucial for survival and necessitate rapid deployment of energy reserves. The amygdala coordinates behavioural adaptations to threats, but little is known about its involvement in underpinning metabolic adaptations. Here we show that acute stress activates medial amygdala (MeA) neurons that innervate the ventromedial hypothalamus (MeAVMH neurons), which precipitates hyperglycaemia and hypophagia. The glycaemic actions of MeAVMH neurons occur independently of adrenal or pancreatic glucoregulatory hormones. Using whole-body virus tracing, we identify a polysynaptic connection from MeA to the liver that promotes the rapid synthesis of glucose by hepatic gluconeogenesis. Repeated stress exposure disrupts MeA control of blood glucose, resulting in diabetes-like dysregulation of glucose homeostasis. Our findings reveal an amygdala–liver axis that regulates rapid glycaemic adaptations to stress and links recurrent stress to metabolic dysfunction.

3:30

Branched-Chain Amino Acids Modulate Sweet Reward Independently Of Neuronal Fgf21 Signaling

Fereshteh Dehghani, Danial Fotros, Zobayda Farzana Haque, Garrett Scott, Maura McKenna, Andrew C Shin

Neurobiology of Nutrition Laboratory, Department of Nutritional Sciences, College of Health & Human Sciences, Texas Tech University, Lubbock, TX, United States

Higher branched-chain amino acid (BCAA) levels are linked to obesity. BCAA restriction stimulates fibroblast growth factor 21 (FGF21), which reduces sweet intake in mice. Whether BCAAs regulate reward through FGF21 remains unclear. We examined the effects of dietary, pharmacological, microbial BCAA

manipulation, as well as the role of neuronal FGF21 signaling (Klb^{ΔSynCre}) on sucrose reward.³⁶ male C57BL/6J mice received control, restricted, or supplemented BCAA diets for 3 months.⁴⁸ mice fed a high-fat diet or regular chow for 12 weeks and received vehicle or BT2 (BCAA-lowering compound; 40 mg/kg ip) daily for 1 month. Another 48 mice fed a HF diet or chow for 8 weeks and received vehicle or BCAA-synthesizing bacterium *Prevotella copri* (5×10⁸, CFU/mouse) in the last 3 weeks. Klb^{ΔSynCre} and Klb^{flox/flox} mice underwent BCAA restriction for 12 weeks. Two-bottle choice, taste reactivity, and progressive ratio tests were performed to assess the hedonic impact (“liking”) and motivation (“wanting”). BCAA-supplemented mice showed 20% higher sucrose intake than control and restricted groups with greater liking and wanting for sucrose. In lean mice, BT2 reduced sucrose intake by 16% without affecting liking or wanting. HF-fed obese mice displayed less liking and wanting for sucrose than lean controls. BT2 did not alter sucrose intake or wanting in obese mice but restored sucrose liking impaired by HF diet. *P. copri* increased sucrose intake by 16% in lean mice, but tended to further reduce sucrose intake, liking, and wanting in obese mice. Klb^{ΔSynCre} mice did not alter food reward behaviors, indicating FGF21-independent BCAA effects. Lowering BCAA levels may reduce appetite and motivation for sweet stimulus, highlighting a novel role for BCAAs in food reward regulation.

3:45

Sweet Taste Phenotypes Are Poor Predictors Of Sugar Intake In Healthy Adults

Alicia Nolden, James Makame

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Individual differences in sweet taste perception are widely assumed to influence sugar intake, yet evidence linking laboratory-derived sweet taste phenotypes to real-world dietary behavior remains inconsistent. Therefore, the objective of this study was to examine the relationship between sucrose-based sweet taste phenotypes, preferences for sweet foods, and dietary intake, specifically total sugar and energy intake. It is hypothesized that perceived intensity and liking of sucrose are associated with liking and intake of sweet foods and beverages. A total of 121 healthy adult participants (aged 18-46; 71.1% female; BMI 24.8±5.0) completed sensory testing and dietary assessments. Sweet taste perception and hedonic liking were evaluated using five sucrose solutions (0.16-0.73M). Intensity ratings were collected using a generalized Labelled Magnitude Scale, and liking was assessed using a generalized bipolar hedonic scale. Participants completed three types of assessments to gain insight into the liking and intake of sweet foods and beverages (24-hour recalls, FFQ, and behavioral assessments). Agglomerative hierarchical clustering of hedonic responses identified three stable sweet-taste phenotype groups based on the combination of reported liking and perceived intensity: low (n=22), medium (n=29), and high (n=63) sweet-liking groups. Contrary to our hypothesis, there was no relationship between sweet-taste phenotypes and total sugar or added sugar intake. However, a weak relationship was observed between sweet-taste phenotypes and self-reported liking of sweet foods and beverages (e.g., cotton candy). Together, these results challenge the translational utility of sweet taste phenotyping for predicting sugar intake among healthy adults.

4:00

SGLT1 Mediates Oral Glucose Sensitivity During Fasting In Humans

Alexa Pullicin, Yixin Jia, Juyun Lim

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Oral glucose sensing is critical for maintaining energy homeostasis, particularly when the body is in an energy-seeking state. We previously showed that suprathreshold concentrations of glucose are perceived as relatively sweeter when fasted compared to fed, and that this effect does not extend to other sweet tastants. To investigate the peripheral mechanism underlying this phenomenon, we conducted a series of experiments. In each experiment, overnight fasted participants attended separate study sessions, and oral detection sensitivity to target compounds, with or without a modulator, was measured before and after consuming a standardized meal to satiety (295–1475 kcal). In the first experiment (N=27), we confirmed our initial finding by testing detection thresholds for glucose, fructose, and sucralose. Results showed that, on average, individuals had lower detection thresholds for glucose when fasted versus fed (paired t-tests; $p < 0.05$), and this effect did not extend to fructose or sucralose. In the second experiment (N=24), we investigated the role of the sodium glucose co-transporter 1 (SGLT1), expressed in gustatory tissue, by measuring glucose detection thresholds under three conditions: 1) normal, 2) pharmacological inhibition of SGLT1 with sotagliflozin, and 3) SGLT1 enhancement with sodium chloride. As expected, under normal conditions, participants were more sensitive to glucose when fasted compared to fed ($p = 0.01$). This effect was abolished following oral pre-treatment with sotagliflozin ($p > 0.05$) and enhanced when NaCl was added to test solutions ($p < 0.01$). These findings demonstrate that SGLT1 is involved in the increased oral sensitivity to glucose when fasted, revealing a mechanism by which the gustatory system contributes to metabolic homeostasis.

4:15

Brain Response Is Influenced By Varying Rates Of Metabolic Response To Carbohydrate Consumption In A Flavor-Nutrient Conditioning Paradigm

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Prior work highlights the sufficiency of post-ingestive glucose sensing to support learned carbohydrate preferences, but whether the rate of metabolism modulates reinforcing potential is unclear. We assessed if metabolic response rate is associated with brain response and behavioral preference in an ongoing randomized, crossover flavor-nutrient conditioning study. Participants aged 18-45y (n=23; target n=64) consumed iso-sweet, novelty flavored drinks containing no calories (sucralose; CS-), 110 kcal maltodextrin (CS+M), and 110 kcal sucrose (CS+S) 6 times each. Indirect calorimetry and blood draws were performed at baseline and

for 1-hr post-consumption. Preliminary analyses indicate blood glucose area under the curve (AUC) was greater for CS+M than CS+S and CS-, and carbohydrate oxidation AUC was greater for CS+S than CS+M and CS- (all $p < 0.01$). Pre-to-post liking and wanting ratings did not differ across conditions, nor did overall neural response (fMRI) across conditions to visual cues or flavor delivery (tested in extinction). There was an interaction between blood glucose AUC and condition in response evoked by the visual cue in the precuneus ($F = 29.72$, $p_{FWE} = 0.003$), driven by an attenuated response for CS+S vs CS- ($t = 7.71$, $p_{FWE} < 0.001$). Given the directional differences in metabolic response for CS+S and CS+M, we performed T contrasts consistent with these opposing metabolic profiles. Blood glucose AUC was associated with a greater cue-evoked response for CS+M > CS+S in the putamen and delivery-evoked response for CS+M > CS+S in the ventrolateral prefrontal cortex and nucleus accumbens (all $t > 5.6$, SVC $p_{FWE} < 0.02$). These findings support the hypothesis that rate of metabolic response to carbohydrate consumption influences neural responses.

Sunday, August 9, 2026

9:00 - 10:00 AM

Regency A

Poster Session 6-1

P401

Behavioral Factors Contributing To High Fat Diet Induced Obesity In Mice

Mason Barrett, Alexxai Kravitz

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While prior studies have demonstrated that increasing the fat content of food drives overeating and obesity in mice, fewer studies have tested how increasing the cost of obtaining high-fat food may control overeating and weight gain. We hypothesized that increasing the cost of high-fat food would limit both over-eating and weight gain in mice. To test this, we designed a home-cage device that dispensed high-fat diet to mice either freely (free access) or after mice completed one nose-poke (nose-poke access), with each nose-poking granting mice access to high-fat diet for sixty seconds. In both conditions, mice were allowed to access the device around the clock and eat as much as they wanted from it. The free-access group gained 2.7g per week, compared with only 1.3g per week in the nose-poke access group (two-tailed independent t-test, $p=0.003$). We concluded that the free availability of calorie dense food promotes overeating, and that imposing a small cost (one nose-poke) reduces high-fat diet intake and weight gain in mice. Here, we extend this work to test if increasing physical or cognitive effort to access high-fat diet might alter weight gain. To increase physical effort, we positioned the high-fat diet location higher in the cage, so mice had to climb to access it. To increase cognitive effort, we required mice to stand still in front of the device for 5 seconds each time they wanted to open it. Our preliminary results show that increasing physical effort did not attenuate weight gain in mice, but increasing cognitive effort did. Our research highlights the importance of environmental modifications as a component of weight management strategies to combat obesity.

P402

Impact Of Hemp Seed Consumption, In The Context Of Western-Style Vs. Low-Fat Diets, On Energy Balance And Memory Function In Rats

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Western-style diets (WD) rich in saturated fat and sugar are associated with metabolic and cognitive dysfunction. Nutritional strategies that mitigate diet-induced metabolic and cognitive impairments are of increasing interest. Dietary hemp seed (*Cannabis sativa* L.; <0.1% tetrahydrocannabinol and <1.6% cannabidiol) contains polyunsaturated fatty acids, dietary fiber, phytochemicals, and other bioactive compounds that may support neurocognitive health through anti-inflammatory effects and mechanisms involving the gut-brain axis. However, the effects of hemp seed consumption, in a form relevant for food applications, on energy balance and memory function across distinct dietary contexts remain unexplored. Male Sprague-Dawley rats (N=48) were assigned to four dietary groups (n=12 per group): control diet (CTL; 10% kcal from fat), CTL supplemented with 3% (w/w) hemp seed (CTL+HS), Western diet (WD; 45% kcal from fat), or WD supplemented with 3% (w/w) hemp seed (WD+HS) for 16 weeks. While we are currently in week 4 of the study, behavioral testing will assess hippocampal-dependent memory function, while open field testing will evaluate anxiety-like behavior. Hippocampal tissue will be analyzed for markers of cholinergic signaling and inflammation. We hypothesize that WD-fed rats will exhibit memory impairments and increased body weight over time, while hemp supplementation will attenuate cognitive deficits, neuroinflammation, and body weight gain. We anticipate that the results from this study will lay the groundwork for better understanding the connections between foods, dietary contexts, and their implications on body weight regulation and gut-brain health.

P403

Improving Reproducibility In Mouse Sodium Appetite Research

Silvia Gasparini¹, Joel Geerling^{1,2}

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Sodium appetite is the homeostatic drive to consume sodium in response to a deficiency. This drive arises gradually during prolonged hypovolemia, the physiologic manifestation of sodium deficiency. Acute fluid loss can accelerate this behavior, but sodium appetite is slow and difficult to study relative to other ingestive behaviors, and our understanding of underlying mechanisms is incomplete. Another major limitation is that while extensive information exists about sodium appetite in rats, relatively limited information exists in mice, which have become the species of choice for genetically targeted experiments, and the small fluid volumes consumed by mice can impede precise and reproducible measurements. We re-analyzed previous data and performed new experiments to compare methods and protocols. We found that injecting the loop diuretic furosemide followed by dietary sodium deprivation elicits stronger and more consistent appetite at 48 hours rather than the previously standard 24 hours. In the same condition, preference for saline relative to water was higher with a 0.9% (0.15 M) NaCl test solution, but appetite-specificity was higher with the 3% (0.5 M) NaCl test solution. We also tested different mineralocorticoid methods and found that infusing

aldosterone directly into the fourth cerebral ventricle is the most potent and specific way to induce salt intake. Finally, we addressed recent mechanistic claims about prostaglandin and angiotensin signaling with evidence that these hormones do not significantly modulate sodium appetite under standard experimental conditions in our laboratory. Incorporating these findings will optimize the reproducibility of future experiments investigating the physiologic, endocrine, and neural-circuit mechanisms of sodium appetite.

P404

Key Drivers Of Energy Drink Appeal Among Adolescents

Travis Masterson¹, Helene Hopfer², Frank Dardis³, Morgan Failla², Callie Millward¹

¹Department of Nutritional Sciences, Penn State, State College, PA, United States, ²Department of Food Science, Penn State, State College, PA, United States,

³Bellisario College of Communications, Penn State, State College, PA, United States

Livestreaming is an increasingly popular online social media activity for adolescents. Energy drinks are the most marketed product on these platforms and are a source of added sugars and caffeine, which have known negative effects on adolescent health. Identifying product attributes that most strongly drive preferences for energy drinks could help to reveal modifiable factors that could be targeted through regulation and counter-marketing. This analysis sought to identify the highest ranked variations for key product factors that were perceived as being most influential for adolescent beverage choice. Adolescents aged 13–17 years (n = 1,471) were recruited nationwide through an online panel. Participants performed a MaxDiff task regarding energy drinks in which they selected the most preferred and least preferred item from a set of options for a variety of product factors: flavors, nutrient composition, ready-to-drink factors, cost, container type, logo factors, packaging colors, marketing factors, and product messaging. Ratio scores were generated for each attribute (0-100) for ranking of preferences. The highest-ranked attributes in these categories were fruit punch flavor, vitamin B content, high quality relative to price, tall slim aluminum cans, neon packaging, association with video games, and messaging emphasizing energy for improved performance. These findings highlight the focal points of adolescents across a variety of product factors. Targeting modifiable factors of products such as marketing strategies, packaging, and price promotions may be helpful in reducing energy drink consumption in this population.

P405

Built Environment Risk Is Associated With Reinforcing Value Of Food And Sensitization In Youth

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The reinforcing value of food (RRV_{food}) is an objective measure of motivation to eat that is a key determinant of energy intake and obesity risk. Repeated exposure to palatable foods can increase RRV_{food} over time through sensitization, which is associated with higher BMI and excess weight gain over time. The purpose of this study is to test the hypothesis that built environment features, including greater access to convenience stores and fast-food establishments and lower access to parks and grocery stores are associated with RRV_{food} and sensitization. Children and adolescents from two studies (n=316) completed measures of RRV_{food}, sensitization, delay discounting, food insecurity (FI), and BMI percentile (zBMI). Home addresses were analyzed with GIS to assess the built environment, including distance to and density of parks, grocery stores, non-grocery stores, restaurants, and fast-food outlets within a 1-mile radius. Variables were classified as high or low using a median split, with lower-risk variables reverse-coded. Risk scores for distance and density were then calculated. Linear models, controlling for age and sex, tested associations between BERisk and zBMI, RRV_{food}, sensitization, FI, and delay discounting. BERisk_{proximity} was associated with greater sensitization to food (p<.001) and adolescent-reported FI (p=0.041). BERisk_{density} was associated with higher RRV_{food} (p=.012) and Sensitization (p<.001). Significant interaction effects between BERisk_{proximity} and BERisk_{density} were observed for zBMI (p<.016), FI (p=.008), and Sensitization (p<.001). These findings suggest the home food environment may influence obesity risk via behavioral reinforcement and contribute to FI in children and adolescents.

P406

Shaping How We Eat: The Barbara J. Rolls Collection Of Human Feeding Studies (1988&Ndash;2025)

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To promote replication and accelerate new discoveries, Penn State Libraries and Dr. Barbara J. Rolls are making all available data (1988-2025) from her career publicly available for future research (~80 studies) as part of The Barbara J. Rolls Collection in ScholarSphere, Penn State's institutional repository. These foundational data were collected as part of in-patient, controlled feeding studies, controlled laboratory studies, and free-living studies in both adults and children. The Collection includes data supporting Dr. Rolls' research on food properties such as macronutrient composition, food form, variety, portion size, and energy density. The Collection also includes data examining microstructure behavior (e.g., eating rate, bite size, switching between foods) during controlled, inpatient meals in adults with eating disorders; comparison of oral vs intragastric nutrient delivery in humans; controlled weight-loss trials; the impact of female hormonal cycles and birth control on eating behavior; and eating behaviors in older populations. Data for each study are curated by Penn State's Research Data Stewardship Department using the PsychDS data standard and published with original documentation and non-proprietary protocol materials, when available. These curated data are then organized into The Barbara J. Rolls Collection with collection-level metadata including descriptions of all studies, a database of measures in each study, and links to archived materials such as grant documents and/or protocol binders. This eases the burden of identifying and harmonizing data across studies for future analysis. The Collection provides a unique resource for secondary analyses, replication, methodological training, and new hypothesis generation.

P407

Characterizing The EEffects Of Retatrutide In Rats On High-Fat Diet On Ingestive Behavior And Liver Transcriptomics

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Retatrutide, a GLP-1R/GIPR/GCGR triagonist, produced 28.3% mean body weight loss over 80 weeks in Phase 3 clinical trials, yet the mechanisms underlying its effects remain under characterized in preclinical rat models. We hypothesize that retatrutide dose-dependently lowers body weight in male Sprague-Dawley rats on high-fat diet (HFD) through reducing meal size and shifting hepatic gene expression toward increased fat oxidation. In a within-subjects counterbalanced design (n=19), HFD-maintained rats received subcutaneous (s.c.) injections of retatrutide (0, 5, 10, 15 nmol/kg), and food intake, body weight, and pica behavior (i.e., kaolin intake) were measured at 3, 6, 24, 48, 72, and 96 h post-treatment. Retatrutide dose-dependently suppressed food intake and body weight, with significant pica behavior observed at the two highest doses. Ongoing meal-pattern analyses are examining whether retatrutide-induced hypophagia is mediated primarily by reduced meal size on HFD after s.c. injections of retatrutide (0, 5, 10 nmol/kg). Data are analyzed by one-way ANOVA with Tukey's HSD. Additionally, separate rats maintained on HFD (n=6/group) received an acute s.c. injection of retatrutide (0, 0 and pair-fed, 10 nmol/kg) 24 h before collecting body weight changes, liver dissections, and trunk blood. Bulk RNA sequencing is ongoing to compare differentially expressed genes in liver using DESeq2, separating the effects of retatrutide from hypophagia on a core metabolic organ. Collectively, these data establish a rat dose-response for retatrutide on ingestive behavior endpoints and provide a framework for how its weight loss efficacy reflects altered meal patterning and intake-independent liver metabolic gene expression, which will inform the development of future weight loss drugs.

P408

Why &Ldquo;Eat Fewer Ultra-Processed Foods&Rdquo; Is Hard: Evidence For Rapid Food Devaluation In Humans

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Despite widespread recommendations to reduce consumption of UPFs many struggle to do so. Preclinical data show high-fat diet exposure decreases the motivational value (devaluation) of nutritionally balanced chow via reward-circuit adaptations leading to transient underconsumption. We tested whether UPF exposure causes devaluation of MPF in humans. In two inpatient randomized crossover feeding studies, weight-stable adults (Study 1: n=20 (10F,10M), age 31.2 ± 1.6yrs and BMI 27 ± 1.5 kg/m²; Study 2: n=18 (7F, 11M), age 38.4 ± 2.6 yrs and BMI 28.7 ± 1.4 kg/m²) consumed ≥7 days of ad libitum UPF followed by nutrient- and duration-matched ad libitum MPF diets, or the reverse. Energy intake (EI) was expressed relative to estimated energy needs (resting expenditure*1.6). Daily EI was compared across diet transitions (UPF-MPF; MPF-UPF) using paired t-tests (α=0.05). Mean weekly UPF EI exceeded energy needs (Study 1: +20.4%±5.9%, p=0.003; Study 2: +31.7%±11.5%, p=0.025), whereas mean weekly MPF EI approximated energy needs (Study 1: +0.13%±4.7%; Study 2: -5.3%±10.4%; p's>0.05). Analysis of daily EI, however, revealed a transient spontaneous decrease in ad libitum MPF EI following UPF-MPF switch reflecting a marked reduction in intake relative to both the end of UPF diet (Study 1: -18.1%, p=0.002; Study 2: -12%, p=0.014) and total energy needs (Study 1: -6.3%±0.06%[SE], 95%CI 6.4%-19.2%; p<0.001; Study 2: -19.0%±11.4%[SE], 95%CI 7.2% - 54.7%; p<0.001). No such effect occurred following MPF-UPF transitions. UPF exposure produced a transient reduction in MPF EI intake in a controlled setting, consistent with dynamic recalibration of food value. UPF-rich diets may increase subjective incentive value of food relative to MPF, potentially contributing to the difficulty of sustaining dietary change in free-living environments.

P409

The Association Between Experiences Of Discrimination And Disordered Eating Is Mediated By Impulsiveness

Laurence J. Nolan, Kaitlyn Miranda, Amy Eshleman
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Disordered eating (DE) is linked to experiences of discrimination and feelings of devaluation. This study had two purposes: to validate the Multiple Devaluation Experience (MDE) tool developed by this research group and to examine whether the MDE or the Everyday Discrimination Scale (EDS) would better predict DE. 188 (n=120 women; 68.1% identified as white) students (BMI M=24.09, SEM=0.37) completed the MDE, EDS, Dutch Eating Behavior Questionnaire (DEBQ), and Barratt Impulsiveness Scale. 92% of participants described some experience with discrimination and devaluation. MDE was positively correlated with both the frequency (EDSf; r=.41, p=.000) and chronicity (EDSc, number of days/year; r=.26, p=.000) of discrimination experience, indicating convergent validity. MDE and EDS were not significantly correlated with BMI. DEBQ subscores were highly intercorrelated, so they were summed to create a composite DE score.

MDE and EDSf, but not EDS_c, were positively correlated with DE in both women (MDE: $r=.41, p=.000$; EDSf: $r=.36, p=.000$) and men (MDE: $r=.39, p=.001$; EDSf: $r=.40, p=.000$). The following were found for women (but not men): DE was positively correlated with attentional impulsiveness (impA; $r=.29, p=.001$) and BMI ($r=.22, p=.014$). EDSf ($r=.45, p=.000$) and MDE ($r=.23, p=.013$) were associated with elevated impA. EDSf was associated with motor impulsiveness (impM; $r=.35, p=.000$). In a regression analysis, EDSf (not MDE) significantly predicted DE in women, controlling for impA, impM, and BMI, $F(1, 113)=5.09, p=.026, R^2=.19$. In women, the association between EDSf and EE (controlling for BMI) was mediated by impA, $F(3, 115)=8.81, p=.000; R^2=.19$; the result was the same for MDE with a lower R^2 . Experiences of discrimination may disrupt attentional processes and lead to DE.

P410

The Effects Of A Transmembrane Mutation Of Adenylyl Cyclase 3 On Food Intake In A Rodent Model

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My lab identified a highly conserved non-synonymous variant in the transmembrane (TM) domain of *adenylyl cyclase 3* (*Adcy3*) that associates with obesity in an outbred rat model. *Adenylyl cyclase 3* is a key enzyme in energy homeostasis and satiety signaling. We created a rat model with a (F122delV123L) mutation in the TM domain of *Adcy3*. We found that male and female rats with this mutation (*Adcy3*^{mut/mut}) showed higher adiposity compared to wild-type (WT) rats. However, the *Adcy3*^{mut/mut} males showed higher food intake, while the *Adcy3*^{mut/mut} females showed decreased energy expenditure. When assessed for emotional behaviors, we found that the *Adcy3*^{mut/mut} males were willing to obtain a food reward, instead of showing depressive-like behavior. This suggests the TM *Adcy3* mutation may be driving feeding behaviors. To further understand how the *Adcy3*^{mut/mut} impacts eating behavior, we evaluated different aspects of eating behavior. We hypothesize that the *Adcy3*^{mut/mut} males will continue to show disrupted homeostatic eating and enhanced hedonic/emotional eating. We further hypothesize that the *Adcy3*^{mut/mut} males will show increased food motivation, with no differences in eating behaviors in the females. Male and female *Adcy3*^{mut/mut} and WT rats (n= 10-12 genotype/sex) were assessed for homeostatic eating, hedonic eating (access to chocolate after being sated), emotional eating (food choice without or without a stressor) and in food self-administration. We found that the *Adcy3*^{mut/mut} females eat significantly more chocolate compared to the WT females after satiation, indicating hedonic eating behavior. There were no differences between MUT and WT females in any of the other eating paradigms. Future studies will determine food intake in the *Adcy3*^{mut/mut} and WT males.

P411

A Rapid Decrease In Phasic Dopamine Precedes The Rapid Change In Salt&Rsquo;S Valence During Satiation Of Sodium Appetite

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Sodium loss induces an innate, highly-conserved, and specific appetite for sodium. However, overconsumption of sodium can lead to hypertension and other life-threatening complications. Thus, understanding how sodium appetite is turned off appropriately during restoration of sodium balance is of interest. Mesolimbic dopamine plays a key role in assigning value to stimuli based on biological needs and is a candidate mechanism. We previously showed that, in sodium deplete rats, intraoral infusions of hypertonic sodium result in robust dopamine release in nucleus accumbens (NAc). Such responses are not seen when animals are sodium replete. The key question addressed here is what exactly happens to phasic dopamine during restoration of sodium balance? We have tackled this by adjusting infusion parameters (sodium concentration and infusion duration) to produce “within-session” satiation while monitoring behaviour and dopamine release simultaneously. Using a machine-learning pipeline to classify observed behaviours, rats (n=20; Long Evans, male and female) exhibited a remarkably rapid and sharp transition in appetitive behaviour across a single session. By simultaneously measuring dopamine release in NAc lateral shell (with fibre photometry recordings of GRAB-DA fluorescence), we show that dopamine responses also decrease rapidly during the session. Realignment of trials to each rat’s behavioural transition point resulted in an even steeper decrease in dopamine about the transition. Cross-correlation of the signals shows that changes in dopamine actually precede decreases in appetitive behaviour by just a few trials. Together, these data support a model in which phasic dopamine responses to ingested sodium cause a rapid updating of appetitive behaviour.

P412

Heterogeneous Gip Receptor Signaling In Mouse Hindbrain Neurons

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A paradox of anti-obesity therapy is that both agonists and antagonists targeting the glucose-dependent insulinotropic peptide receptors (GIPR) enhance the weight-loss efficacy of GLP-1 receptor agonists. Recent evidence suggests that GIPR agonism and antagonism may recruit separable neuronal populations. However, it is unclear whether heterogeneity within the cellular response to GIP contributes to the complex role of GIPR-mediated metabolic regulation. We hypothesized that GIP-expressing populations in the area postrema (AP; GIPR^{AP}) and nucleus of the solitary tract (NTS; GIPR^{NTS}) are heterogeneous and use ex vivo electrophysiology and calcium imaging (n=4-8 mice per experiment) to directly examine the cellular mechanisms underlying GIP action. GIP did not significantly alter membrane potential or action potential firing but increased intracellular calcium ($p<0.05$). Calcium imaging revealed distinct subpopulations of GIPR^{AP} that exhibited either transient activation followed by suppression, or slower sustained activation. GIPR^{NTS} neurons primarily exhibited sustained

responses. Repeated GIP application attenuated responses, consistent with receptor desensitization. GIP-evoked calcium signals persisted during synaptic blockade, indicating a cell-autonomous mechanism. PKA inhibition prevented GIP-induced activity, while inhibition of Gq signaling significantly attenuated, but did not abolish the calcium response, indicating the engagement of both G_s and G_q-coupled pathways. These findings demonstrate that GIPR signaling in hindbrain neurons is heterogeneous and this signaling complexity provides a cellular framework for how GIPR modulation may differentially influence neural circuits.

P413

Transcriptomic And Functional Evidence Of Glp-1R Expression In Non-Dopaminergic Vta Neurons

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Over 73% of the United States population is overweight or obese, increasing the risk of life-threatening conditions such as type 2 diabetes mellitus and cardiovascular disease. GLP-1 receptor agonists (GLP-1RAs) effectively treat obesity, yet over half of patients discontinue within one year due to side effects such as nausea. This renders available GLP-1RAs ineffective for many patients and highlights a need for more tolerable medications that produce weight loss without aversive side effects. Previous work demonstrated that injection of GLP-1RAs into the ventral tegmental area (VTA) reduced food intake and drove weight loss in rodents without malaise. However, the cellular identity of VTA GLP-1R-expressing cell populations that these GLP-1RAs might act on is poorly understood. We evaluated publicly available spatial transcriptomic datasets to characterize GLP-1R-expressing populations. In the VTA, the GLP-1R was expressed primarily in non-dopaminergic neurons, suggesting that GLP-1 acts indirectly on dopamine neurons. Surprisingly, GLP-1R-expressing neurons in the VTA were rare, accounting for <1% of total neurons. To functionally probe GLP-1R effects in the VTA, we optogenetically stimulated GLP-1 expressing neuron terminals in the VTA of *Gcg-iCre* mice (n=5). Consistent with prior work using pharmacological GLP-1RAs, optogenetic stimulation of VTA-GLP-1 terminals also reduced food intake in an overnight-fasted 30-minute feeding assay. These findings suggest VTA GLP-1R signaling can suppress food intake through a circuit distinct from more widely studied brainstem mechanisms that reduce feeding but also engage malaise.

P414

The Effects Of Long-Term Semaglutide Treatment On Accumbal Dopamine Activity.

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Millions of people are treated with semaglutide to successfully induce weight loss. However, despite widespread use and profound health benefits, response to treatment varies across individuals. This suggests that ongoing semaglutide treatment drives varied outcomes in behaviour and the underlying brain motivation circuits. However, the extent to which such changes are associated with semaglutide-induced weight change remain unclear. Preliminary data suggests nucleus accumbens (NAc) dopamine decreases with semaglutide treatment, specifically during food seeking. Here we explore how long-term (20 week) semaglutide treatment drives differences in motivated behaviour, physical activity, and underlying dopamine dynamics in the NAc. We express GRAB-DA in the NAc and use in vivo fiber photometry to record dopamine activity during a food motivation task in a cohort of 21 mice exhibiting a spectrum of semaglutide-induced weight change. The results of this work will shed light on the relationship between semaglutide-induced weight change, food motivation, and NAc dopamine dynamics.

P415

Semaglutide Drives Weight Loss Through Camp-Dependent Mechanisms In Glp1R-Expressing Hindbrain Neurons

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Glucagon-like peptide 1 receptor (GLP1R) agonists, such as semaglutide, drive weight loss by binding to GLP1Rs—classically described as G_s -coupled G-protein-coupled receptors—in the brain; however, the intracellular signalling mechanisms underlying these effects remain poorly defined. Here, we find that semaglutide engages both G_s - and G_q -dependent signalling pathways in Glp1r-expressing neurons in the area postrema (AP^{Glp1r}), the primary site of semaglutide action in the brain, and differentially regulates neuronal activation across distinct neuronal clusters. Semaglutide also drives graded increases of the essential secondary messenger cyclic adenosine monophosphate (cAMP) in AP^{Glp1r} neurons through the G_s pathway. Inhibition of the cAMP-degrading enzyme phosphodiesterase 4 (PDE4) enhances and sustains these cAMP responses, and disruption of G_s or cAMP signalling in AP^{Glp1r} neurons abolishes semaglutide-induced weight loss and downstream brain-wide activation. Our systematic characterization of semaglutide's signalling mechanisms in the hindbrain reveals the intracellular signalling architecture through which semaglutide engages cAMP and calcium to regulate body weight, providing avenues for improving obesity therapeutics.

P416

Sex-Specific Differences In Baseline Running And Food Intake Predict Susceptibility To Activity-Based Anorexia

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Anorexia nervosa (AN) is a life-threatening psychiatric disorder marked by severe weight loss due to a combination of voluntary food restriction, oftentimes a co-occurring increase in physical activity. Despite the high global mortality rate, the neural mechanisms remain poorly understood. Preclinical studies investigate these mechanisms using the activity-based anorexia (ABA) model in mice, which combines limited food access with voluntary wheel running, inducing hyperactivity, self-starvation, and rapid weight loss in a subset of subjects. Not all individuals who diet and exercise develop AN; similarly, only a subset of rodents in the ABA exhibit rapid weight loss. Yet, no phenotypic or neural indicators exist to identify ABA susceptibility before weight loss, thus limiting early intervention. We developed a supervised machine-learning algorithm with longitudinal body weight change in ABA that revealed sex-specific differences in baseline behavior. While ABA-susceptible female mice exhibit higher baseline wheel running compared to ABA-resilient females, this is not observed in males. In contrast, ABA-susceptible male mice consume less food before food restriction, which is not observed in females. A second predictive model trained on baseline voluntary running and food intake data leveraged these signatures to classify ABA-susceptibility before severe weight loss. Ongoing studies using closed-loop optogenetic activation of AgRP neurons before food restriction during hyperactive (female) or underconsumption (male) bouts will determine if modulating AgRP circuits can rescue ABA-susceptible animals before weight loss. This framework thus identifies early indicators of ABA-susceptibility inform better diagnosis and therapeutic strategies.

P417

Glucagon-Like Peptide-1 Receptor Agonism Enhances Excitatory Drive In The Olfactory Bulb And Piriform Cortex

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Olfactory cues in the environment can signal food availability and drive food-seeking behaviors. 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, the precise circuit physiology has not been resolved. We first considered how GLP-1 receptor (GLP-1R) agonism would modulate sensory representations in the OB using *in vivo* multiphoton microscopy. Preliminary data indicate that systemic semaglutide injections (3 nmol/kg) in mice (n=3) decrease odor-evoked activation of GLP-1R-expressing neurons ($D=0.06$, $p<0.01$; putative periglomerular cells), which then result in an increase in odor-evoked mitral cell activity ($D=0.14$, $p<0.01$). Next, we considered how GLP-1R agonism affects the balance between excitation and inhibition in the piriform cortex (PC), where odor identities and their associations with food are established. We found that GLP-1R agonism (Exendin-4, 1 μ M) increased excitatory drive to PC pyramidal neurons (n=10) by increasing spontaneous excitatory postsynaptic current frequency (EPSC; $b=4.17$, $p<0.01$), increasing spontaneous EPSC magnitude ($b=39.45$, $p<0.01$), and decreasing evoked inhibitory postsynaptic current magnitude ($t=3.15$, $p=0.02$). However, GLP-1R agonism did not affect the cell-intrinsic properties of pyramidal cells. GLP-1R may reside within the local inhibitory neurons within the PC, as reporter expression in GLP-1R neurons is morphologically consistent with inhibitory neurons. Together these findings are consistent with a model in which decreased local inhibition in the OB, increases mitral cell output, thereby increasing PC activity and reconfiguring sensory representations.

P418

Lateral Hypothalamic Circuits To The Paraventricular Thalamus And Medial Septum Differentially Control Consumption And Food Seeking

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Feeding is a complex process that involves multiple stages, including integrating internal signals such as hunger or motivation, food seeking, and food consumption. The lateral hypothalamus (LH) is a critical regulator of food intake. GABAergic neurons in the LH (LHGABA) are involved in food consumption, motivation and food-seeking behaviors. These LHGABA neurons project to multiple downstream areas including the paraventricular thalamus (PVT) and the medial septum (MS), both of which are also involved in feeding behavior. We hypothesize that distinct aspects of feeding behavior are controlled by distinct LHGABA output circuitry. We used Vgat-Cre mice and induced expression of channelrhodopsin-2 (ChR2) to selectively activate LHGABA→PVT (n=14) or LHGABA→MS (n=12). We found that activation of both projections induced licking and feeding behavior regardless of stimulus valence. However, in the absence of food, activation of the LHGABA→PVT pathway evoked stronger consummatory behavior compared to LHGABA→MS activation. In contrast, activation of LHGABA→MS produced more pronounced food-seeking behavior. Using retrograde tracing, we found that LHGABA neurons projecting to the PVT and MS form distinct pathways with minimal collateralization. As LHGABA projections induce inhibition of these targets, direct somatic activation in Vglut-Cre mice (PVTvglut (n=5) and MSvglut (n=6)) predictably reduced food consumption. Downstream pathways from PVT to central amygdala (CeA) and MS to preoptic area (POA) recapitulate these effects, demonstrating biased control of food seeking by the LH-MS-POA pathway and consummatory behavior by the LH-PVT-CeA pathway. These results suggest distinct aspects of the feeding repertoire are coordinated by parallel efferent LH pathways.

P419

nEural Networks Underlying Diminished Food Motivation Following Variable Food Access In Mice.

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Eating disorders (ED) are deadly psychiatric illnesses characterized by severe and persistent disturbances in feeding behaviors. Recent work has suggested that food insecurity (FI) at any stage of life is a positive risk factor for ED development, yet the underlying neurobiology driving this increased propensity is not understood. Here, we sought to determine how unexpected food availability impacts mouse behavior, with the goal of establishing a FI behavioral paradigm in mice that can be used to investigate the impact of FI on maladaptive feeding behaviors during and after unpredictable food access. Leveraging the Feeding Experimentation Device 3 (FED3), we generated random timeouts between food pellet dispensals such that individuals had no food for unpredictable amounts of time. Despite a return to baseline conditions in which all mice had unlimited access to food, mice that previously experienced variable food access (Random Feed) continued to demonstrate diminished food intake, with reduced motivation for food. Behavioral testing following unexpected food availability reveals an increase in exploratory behavior, suggesting that prior variable food access does not drive anxiety-like behaviors. To better understand the neural influences underlying reduced motivation for food pellets, experiments are ongoing to identify the neural networks active across groups following operant conditioning for food. Together, these studies suggest that unpredictable access to food can influence the onset of maladaptive feeding behaviors and shifts in food motivation.

P420

Altered Sensitivity To Cholecystokinin's Satiating Effects In The TgF344 Alzheimer's Rat Model

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Gut health is associated with Alzheimer's disease (AD) and related dementia. Our previous work revealed that gut vagus nerve ablation in rats impairs hippocampal spatial and episodic memory. Together these findings suggest a potential link between vagal signals and memory disruption. TgF344-AD rats, a transgenic model of AD, exhibit increased body weight and food intake when compared to wild types (WT). Here we investigated whether TgF344-AD rats exhibit altered sensitivity to gut-derived vagal signals before the onset of AD pathology. To test this, 40 WT and TgF344-AD rats were injected intraperitoneally with either 3.0ug/kg CCK or vehicle after a 24 hour fast. High fat, high sucrose diet (HFHS) was given immediately after the injection, and food intake was measured at the 30- and 60-minute mark. Contrary to our hypothesis, AD rats showed an increased sensitivity to CCK, consuming less relative to WT at both time

points. To determine if this extends to other appetite-suppressing gut hormones, we performed a similar test using the GLP-1 analog exendin-4. Rats were injected with either 1.5ug/kg exendin-4 or vehicle, and HFHS intake was measured at 1h, 3h, 6h, and 24h. There was no significant difference in food intake across genotype and time points, suggesting that CCK, but not GLP-1 sensitivity is significantly altered in AD pathology. Together, these results begin to characterize the underlying intricacies of gut disruption and vagal signaling in AD, important factors in assessing patient comfort and care.

P421 **Dopamine Dynamics In An Associative Learning Paradigm Are Modulated By Morphine Through Intoxication And Withdrawal.**

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Opioids act on the mesolimbic dopamine pathway and chronic exposure can alter this circuit, with effects on motivated behaviors. Opioids have been shown to alter behavioral sensitivity to reward during intoxication and withdrawal. To assay reward sensitivity independent of behavioral effects of intoxication, we used an associative learning paradigm to examine mesolimbic dopamine release in response to non-contingent brain stimulation using *in-vivo* fiber photometry through chronic morphine administration and withdrawal. The dopamine sensor dLight1.3b was injected and a fiber optic cannula was implanted into the nucleus accumbens (NAc) of Long Evans rats (n = 9). A bipolar stimulating electrode was implanted in the medial forebrain bundle (MFB). Within a session, each trial consisted of MFB stimulation preceded by an auditory cue. Five different stimulation frequencies were used ranging from 0 to 141 Hz, each paired with a unique cue. Sessions consisted of 10 blocks of 5 trials, with cue-stimulation pairings presented in a randomized order. Animals were trained on the task for 10 sessions. Next, morphine was administered to a subset of animals immediately prior to the session for 7 days, on alternating days to allow for measure of acute withdrawal between administrations. Responses to each cue and stimulation were analyzed by trial type and session day. Cue responses scaled with predicted frequency, and became more discriminable across training. Responses to predicted stimulation diminished over the course of training. Morphine administration augmented responses to stimulation and cues at high frequencies. During acute withdrawal, responses to stimulation remained elevated over saline control animals, while cue responses returned to control levels.

P422 **Positive Allosteric Modulation Of Mglur1 Reduces Cue-Induced Food-Seeking In Obesity Prone Rats**

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Pavlovian food cues can powerfully influence behavior and promote overeating. Alterations in nucleus accumbens (NAc) activity increase susceptibility to weight gain by enhancing sensitivity to motivational properties of food cues. Within the NAc, excitatory transmission is mediated by AMPA receptors (AMPA), including calcium-permeable AMPARs (CP-AMPA). We found that cue-induced food-seeking (PIT) depends on NAc CP-AMPA and is enhanced in selectively bred obesity-prone (OP) rats. Here, we determined whether treatment with a positive allosteric modulator (PAM) that decreases CP-AMPA would reduce PIT. PAMs enhance activity of an endogenous ligand at its receptor and are more amenable therapeutics than direct agonists. PAMs of the metabotropic glutamate receptor 1 (mGluR1) decrease CP-AMPA mediated transmission by enhancing CP-AMPA internalization. Thus, we hypothesized that treatment with an mGluR1 PAM (10 mg/kg, s.c.) would decrease PIT. Studies used OP rats (n=16/ sex), as they show robust PIT that relies on NAc CP-AMPA. We found that an mGluR1 PAM robustly decreased PIT in males, but failed to blunt PIT in females, despite leaving conditioned approach intact in both sexes. This is consistent with our hypothesis and reductions in PIT following NAc CP-AMPA blockade in males, as well as results from our lab showing sex differences in diet-induced CP-AMPA plasticity. Ongoing work will confirm that the mGluR1 PAM decreases NAc CP-AMPA-mediated transmission, and address sex differences in the expression of PIT using LabGym, a machine-learning based behavioral analysis tool. Together, these studies will provide support for potential development of mGluR1 PAMs as a viable therapeutic approach to reduce the capacity of food cues to drive food-seeking behavior.

P423 **Ventral Hippocampus → Accumbens *Grin3A* Knock-Down Elicits Excessive Inhibitory Control And Increases Susceptibility To Activity-Based Anorexia.**

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Anorexia nervosa (AN) elicits severe weight loss due to voluntary food restriction. Activity-based anorexia (ABA; 22h food restriction + running wheel) models these features in mice, but AN neurobiology remains obscure. Evidence implicates ventral hippocampus-nucleus accumbens projections (vHip→NAc) in AN behaviors. vHip→NAc integrates internal satiety signals and contextual food cues to regulate inhibitory control over eating, and ABA susceptibility is associated with vHip dendritic spine density/stability, suggesting inappropriate vHip synaptic maturation may underlie AN behaviors. Intriguingly, the NMDA receptor subunit gene *Grin3A* is retained in adult vHip, acting as a negative regulator of synaptic maturation. We hypothesized that vHip→NAc selective shRNA knock-down of *Grin3A* expression would drive inappropriate maturation and produce inflexible, maladaptive eating behaviors. Relative to controls, we observed a ~2.3-fold decrease NMDAR EPSC decay constant (τ ; n=4; t test, p=0.01), consistent with mature, GluN2A-dominant receptor composition. Behaviorally, 3A-KD mice exhibited a striking reduction in contingency-dependent impulsive actions during fixed-ratio operant sessions (~3.5-fold fewer non-reinforced FR5 responses; n=11; t test, p=0.03), consistent with AN-like excess inhibitory control. 3A-KD mice also showed greater ABA susceptibility (n=15/17 3A-KD, 8/12 ctrl; log-rank p=0.048), with ~2.3-fold higher weight loss exclusion threshold hazard (Cox regression), reaching threshold 35% faster (log-norm ratio 0.64, p=0.04; RMST Δ =-1.9d). Thus, *Grin3A*-dependent synaptic immaturity in vHip→NAc supports appropriately flexible feeding behavior, and vHip→NAc metaplasticity factors may represent promising targets for AN pharmacotherapeutics.

P424

A Ventral Hippocampal To Prelimbic Cortex Circuit Modulates Impulsive Action But Not General Consummatory Behavior In Male Rats.

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Impulsivity is associated with obesity and binge-eating disorder. We recently demonstrated that the ventral hippocampus (field CA1; CA1v) is critical for impulse control in male, but not female rats. To investigate whether the prefrontal cortex (PL) of the medial prefrontal cortex is a downstream mediator of impulse control by CA1v neurons, we injected a retro-Cre virus into the PL and a Cre-dependent inhibitory DREADD virus in the CA1v in male rats to allow for reversible disconnection of this circuit. The rats (n=16) were trained for five weeks in the differential reinforcement of low rates of responding test (DRL-20), a behavioral test of impulsive action where rats learn to withhold lever pressing for 20 seconds to obtain a palatable food pellet. Testing occurred using a counterbalanced within-subjects design with vehicle and the DREADD agonist Deschloroclozapine (DCZ) (100mg/kg; IP) with a 3-day washout period between treatment conditions. Contrary to our initial prediction, we saw that DCZ treatment yielded significantly higher efficiency scores and increased inter response time intervals relative to vehicle, results consistent with increased cognitive control over impulsive action following CA1v-PL disconnection. Next we measured chow consumption in a BioDAQ food intake monitoring system using a within-subjects vehicle/DCZ counterbalanced design. Results revealed no significant differences in total grams consumed, average meal size, or meal number between conditions. This suggests that the DRL results may be based on reduced impulsivity with no changes in food motivation, although this hypothesis requires further testing. Overall, we demonstrate that the CA1v-PL circuit plays a modulatory role in impulsive action but does not affect general consummatory behavior.

P425

Intergenerational Inheritance Of Food PreferenceLeo Tornes^{*1}, Ahyun Jung^{*1,2}, Mohammed A. Al-Sabeh¹, Lindsey A. Schier¹¹Department of Biological Sciences, University of Southern California, Los Angeles, CA, United States, ²Department of Biology, University of Pennsylvania, Philadelphia, PA, United States

The transmission of non-genetic information across generations can shape adaptive fitness and survival phenotypes in response to environmental conditions. While early-life dietary environments, including in utero and lactational exposures, shape neurobiological and behavioral systems underlying metabolic regulation, it remains unclear whether these traits can also be indirectly inherited. Here, we tested whether a learned nutrient preference, which enables mice to rapidly identify calorically efficient food sources by taste, is transmitted from parent to offspring through an indirect inheritance mechanism. Adult female and male mice consumed metabolically distinct simple sugar solutions (glucose and fructose) as dietary supplements or control solutions prior to mating. Mice exposed to the sugars developed a strong preference for glucose over fructose. One week later, the conditioned female mice were mated to naïve male mice, and the conditioned male mice were mated to naïve female mice. Offspring were subsequently assessed for their glucose versus fructose taste preference as adults. Across groups, female offspring of the unconditioned (control) dams and sires licked more to fructose than glucose, while female offspring from the sugar-conditioned dams and sires licked at comparable levels for the two sugars, suggesting that parental nutritional conditioning alters offspring appetitive and consummatory responses to oral sugars. Ongoing studies are assessing differences in taste receptor expression profiles and monitoring how readily offspring learn about sugars. Collectively, these findings advance understanding of how parental experience shapes neural circuits, taste signaling, and motivational pathways involved in nutrient preference and feeding behavior.

P426

Tirzepatide Reduces Fentanyl Taking And Seeking In Male And Female RatsXinming Zhang^{1,2}, Christian E. Edvardsson³, Megan C. Dalalo^{1,2}, Micah Ford^{1,2}, Elisabet Jerlhag³, Heath D. Schmidt^{1,2}¹Department of Biobehavioral Health Sciences, School of Nursing, University of Pennsylvania, Philadelphia, PA, United States, ²Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States, ³Department of Pharmacology, Institute of Neuroscience and Physiology, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

In 2022, an estimated 60 million people worldwide engaged in non-medical opioid use, and opioids account for approximately 450,000 of the 600,000 global drug-related deaths annually. Relapse rates associated with current Opioid Use Disorder (OUD) treatments remain discouragingly high, highlighting the need for novel medications. Emerging studies indicate that satiety factors, including glucagon-like peptide-1 (GLP-1), modulate appetitive and relapse behaviors associated with addictive drugs. While GLP-1 receptor (GLP-1R) agonists attenuate drug-seeking in rodents, their clinical utility is often limited by adverse gastrointestinal (GI) effects. Glucose-dependent insulinotropic polypeptide (GIP), another gut-derived peptide hormone, has an antiemetic effect and, when combined with GLP-1R agonism, may improve both efficacy and tolerability. This study tested the hypothesis that tirzepatide, a dual GLP-1R/GIPR agonist, would decrease voluntary drug-taking and -seeking behaviors at doses that do not produce nausea or malaise-like effects in fentanyl-experienced rats. Male and female Sprague-Dawley rats self-administered fentanyl (1.25 µg/kg-1, i.v.) on a fixed-ratio schedule. Once intake stabilized, rats were pretreated with vehicle or tirzepatide (3.0 or 30.0 nmol/kg, s.c.) prior to a self-administration session. Tirzepatide dose-dependently attenuated fentanyl self-administration in both sexes. Fentanyl taking was then extinguished, and tirzepatide pretreatment during abstinence attenuated subsequent reinstatement of fentanyl-seeking. Doses that suppressed drug taking and seeking also reduced food intake but did not produce malaise-like effects. These preclinical findings support further studies of dual GLP-1R/GIPR agonists for reducing opioid-mediated behaviors.

P427

Dio Rats Chronically Treated With Semaglutide Overconsume Sucrose And A Cafeteria DietCarolina R. Cawthon^{1, 2}, A. Valentina Nisi^{1,3}, Ginger D. Blonde³, Carel W. le Roux⁴, Alan C. Spector^{1,3}

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We previously found, compared with vehicle (VEH)-treated controls, rats that undergo semaglutide (SEMA) dose escalation (ESC) followed by maximum-dose maintenance (MAINT) eat less chow, weigh ~16% <controls, and overconsume and show greater preference for lower sucrose concentrations, vs chow. However, rats with diet-induced obesity (DIO) could provide a better model of SEMA use for weight loss in humans. Here, we gave male SD rats chow + high-fat high-sugar diet for 10 weeks to induce DIO. Rats were then moved into a 5-item food choice monitor and, after 4 d, were switched to a chow-only diet. Once BW stabilized (10 d), rats began VEH (n=8) or SEMA ESC (7-70 μ g/kg sc over 10 d, n=7) followed by MAINT (70 μ g/kg/d). At MAINT Day 10, SEMA rats weighed 14.2% <VEH with lower chow intake characterized by decreases in meals/d, meal size, and eating rate. Rats were then offered 4% and 24% sucrose solutions (crossover, 21 h/d, 4 d/conc) vs H₂O. The SEMA-treated rats overconsumed 4% sucrose and did not underconsume 24%. After 8-d with only chow, rats were given a palatable cafeteria diet (8 d). SEMA rats strikingly increased energy intake to >1.5X baseline, due purely to increased meal size, with values not unlike VEH rats. Notably, relative macronutrient intake differed little between SEMA- and VEH-treated rats. The behaviors of these DIO SEMA rats generally corresponded to the previous study using chow-raised rats, as did their persistent weight loss despite the waning of SEMA-induced suppression of energy intake. These data support our ongoing assertion that the behavioral consequences of chronic vs acute SEMA treatment differ and challenge the prevailing view that SEMA decreases the reward value of palatable food, though this should be explicitly tested.

P428

Vitamin B1 Supplementation Attenuates Exercise Fatigue And Central Metabolic Alterations In A Hfd-Induced Thiamine Deficiency Mouse Model

Elena Kozlova¹, Crystal Luna¹, John Leano¹, Gayatri Raut¹, Jose Martinez-Lomeli¹, Patrick Degnan², Poonamjot Deol¹, Frances Sladek¹, Margarita Curras-Collazo¹

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Dietary deficiencies in vitamins such as thiamine (Vitamin B1) are common even in developed countries and can have a range of deleterious health effects. The trend in Vitamin B1 deficiency coincides with increased fat consumption in the American diet, particularly of soybean oil, the most widely consumed cooking oil in the U.S. which is a component of many processed foods. Here, we hypothesize that the concurrent malnutrition caused by a soybean oil-based high fat diet (SO-HFD) and a physiological deficiency in thiamine can impact regional gene expression in the brain and behavior. To test this, C57BL/6N male mice (N=10-12 per group) were fed either a low-fat chow (OSD) or an SO-HFD, with or without supplementation with 640 mg/kg of the thiamine analog thiamine tetrahydrofurfuryl disulfide (TTFD), for 18 weeks. Mice were subjected to a series of behavioral tests designed to evaluate cognition (passive avoidance test, PAT), strength (modified grip strength test, MGS), exercise endurance (treadmill test, EE), and locomotor/habituation activity (open field test, OFT). Our results showed no difference across groups on the PAT. On the MGS test, the force generated when normalized to body weight was lesser on all test days for SO-HFD as compared to OSD (p<0.05-0.0001). The TTFD supplementation improved MGS only in the SO group (p<0.05). On EE, OSD ran significantly longer before exhaustion as compared to SO (p<0.05-0.001). For one subset of animals TTFD supplementation improved the EE score in SO but not OSD (p<0.05-0.001). During the one-hour OFT, distance traveled decreased over time for both TTFD-supplemented groups only (p<0.05-0.01), indicating improvement in habituation/learning. Transcriptomic analysis of the hypothalamus and hippocampus from these mice revealed differentially expressed genes (p<0.05) that may contribute to alterations observed in the behavioral tests. Metabolomic analysis indicated that TTFD ameliorated the deregulatory effects of SO diet on brain metabolites. Our results indicate that TTFD supplementation may prevent deleterious health effects from thiamine deficiency produced by intake of SO-rich high fat diet.

P429

Establishing The New Zealand Obese Mouse As A Model For Weight-Cycling In Polygenic Obesity

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The sustained negative energy balance required for body weight (BW) loss triggers a compensatory reduction in resting metabolic rate (RMR), the largest component of total energy expenditure (TEE). Reduced RMR contributes to BW loss plateaus and increases susceptibility to BW regain, resulting in weight-cycling, a process by which a person repeatedly loses and regains BW. The New Zealand obese (NZO) mouse is a polygenic model of obesity which replicates two behaviors that promote obesity: hyperphagia and physical inactivity. The study objective was to replicate one weight cycle in NZO mice to assess their viability as a model of weight-loss induced reductions in TEE and RMR. We hypothesized that weight-reduced NZO mice would display a sustained reduction in TEE and RMR. To test this, obesity was induced in female NZO mice (n=16) via ad libitum low fat diet (LFD). At obesity, mice were assigned to one of two groups: weight-cycled mice (WC, n=9), which underwent caloric restriction to induce BW loss, and control mice (n=7), which continued to receive ad libitum LFD. Restoration of ad libitum LFD facilitated BW regain. Body composition and TEE were quantified at baseline, peak obesity, post BW-loss, and post BW-regain. Total energy expenditure, RMR, FI, and BW were adjusted for repeated measures and interaction between time point and treatment group using linear mixed models and estimated marginal means (EMM). After reintroduction of LFD, control and WC mice had equivalent FI (EMM: p=0.91). However, WC mice

had lower TEE and RMR (EMM: TEE, $p=5.0E-3$; RMR, $p=5.6E-3$) resulting in greater BW gain (EMM: $p=1.2E-8$). These data suggest that suppressed RMR post-weight loss enhances susceptibility of NZO mice to BW regain, making this strain a valuable model to study weight cycling.

P430

Semaglutide Alters Sugar Preference Dynamics Without Compromising Glycemia And Weight Maintenance

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Glucagon-like peptide-1 receptor (GLP1r) agonists, such as semaglutide (SEMA), have transformed the treatment of type 2 diabetes and obesity. Although SEMA's appetite-suppressing effects are thought to contribute to its therapeutic efficacy, its impact on food preference, particularly for sugars, remains poorly understood. Intriguingly, emerging evidence suggests that extended SEMA treatment may paradoxically increase sugar consumption. Considering this has the potential to undermine SEMA's long-term metabolic benefits, we investigated how prolonged SEMA treatment alters the hedonic appeal of sugar and influences metabolic outcomes under conditions of acute and chronic access to sugar in lean mice. After 10 days of SEMA treatment, we observed a reduction in body mass and increased sugar appetite in a short-term intake test. Interestingly, despite comparable weight loss, caloric intake, and blood glucose levels, these SEMA-treated mice exhibited elevated GLP1r in the taste buds and increased dopamine D2 receptor transcript in the ventral striatum relative to pair-fed controls. However, with regular access to sugar, SEMA-treated mice gradually normalized their intake and ultimately consumed less sugar than pair-fed controls, enabling them to maintain stable body weight throughout treatment. Moreover, after 12 days of continuous sugar access, SEMA-treated mice retained exceptional glucose tolerance and showed no detectable transcriptomic changes in the taste buds or the striatum. Collectively, these findings show that chronic GLP1r agonism reprograms key intermediaries in the taste-reward axis, which drives acute sugar overconsumption, but these SEMA-induced adaptations dissipate with prolonged access to sugar, thereby preserving metabolic fitness.

P431

Glp-1 Analogue, Semaglutide, Affects Male And Female Reproductive Systems In Rats.

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Semaglutide (SEMA) is a GLP-1 analogue approved for treatment of obesity. The effects of SEMA on body weight are well established, whether and how these blockbuster drugs affect the reproductive system is poorly understood. To address this gap, we investigated the impact of chronic, 4-week treatment with SEMA on gonads as well as circulating reproductive hormones in diet-induced obese male and female Sprague-Dawley rats ($n=10-12$ per sex/group). We found that GLP-1R is expressed in ovaries and testes, allowing a direct effect of SEMA. To disambiguate the direct effect of the drug from potential downstream effects of weight loss, and ensuing improvements in metabolism, produced by the drug we evaluated pair-fed (PF) controls. Pair-feeding and SEMA increased indicators of fertility such as sperm concentration and motility parameters, in males. Morphological analysis of male and female gonads also indicated increased fertility via structural changes. Circulating pituitary luteinizing hormone (LH) was decreased in PF and SEMA males. In contrast, in females SEMA but not PF tended to decrease plasma LH. Circulating sex steroids were measured by LC-MS. Restricted feeding was associated with increased estradiol levels and increased testicular aromatase expression, along with reduced testosterone, in males. This shift in increased testosterone to estrogen conversion was attenuated by SEMA. In contrast, in females, levels of progesterone and pregnenolone were robustly affected. This study highlights broad SEMA-specific, as well as weight loss induced but rescued by SEMA, effects at transcriptional, functional, and systemic levels on the reproductive systems of both sexes.

9:00 - 10:00 AM	Regency Foyer
Exhibits & Coffee Break	
10:00 - 11:30 AM	Regency B
Symposium 4: Ingestion on a Budget	

Chair(s): Laura Rupprecht

10:00

The Crunchometer: A Low-Cost, Open-Source Acoustic Analysis Of Feeding Microstructure

Ranier Gutierrez

CINVESTAV del IPN, Mexico City, Mexico

Elucidating the neuronal circuits that govern appetite requires a detailed analysis of the microstructure of solid food consumption. A significant barrier in this field is that existing techniques for monitoring feeding are either prohibitively expensive, limiting their use, or lack the high temporal resolution necessary to align feeding events with neuronal activity. To overcome this, we developed the Crunchometer, a low-cost, open-source acoustic system that uses computational algorithms to create high-resolution feeding ethograms. We validated the system by monitoring feeding across different energy states (hunger/satiety) and by demonstrating that the anti-obesity drug semaglutide suppresses food intake and reduces preference for a high-fat diet. Crucially, the Crunchometer integrates seamlessly with in vivo neural recordings in freely behaving mice. By pairing our system with electrophysiology in the Lateral Hypothalamus (LH), we identified novel “meal-related” neurons that track entire meals rather than individual feeding bouts. Using calcium imaging, we further revealed that solid food consumption strongly modulates LH GABAergic and glutamatergic neurons. We also found that distinct LH neuronal ensembles encode the consumption of solid food versus liquid sucrose. The Crunchometer is thus a powerful and accessible tool for precisely dissecting the neural correlates of naturalistic feeding behavior.

10:30

Doing More With Less: Open-Source Tools Reveal Hidden Structure In Feeding And Motivation

Bridget Matikainen-Ankney

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Open-source behavioral tools are fundamentally reshaping how we study ingestive behavior. Tools like FED3, FORCE, and home-cage activity monitoring systems are making the field more accessible, and generating data sets that are flexible and rich. These tools offer simple and adaptable methods to measure food-seeking and effort-based behaviors in a variety of experimental contexts. Assays using FED3 and FORCE, in particular, have been valuable for investigating motivated behaviors in mouse models of diet-induced obesity and weight loss. These platforms enable rapid data collection and efficiently allow iterative experimentation, which is particularly beneficial when establishing a research program. Another key strength of these tools is their ability to produce datasets that extend far beyond their initial applications. For instance, operant feeding assays with FED3 do more than track responses within a reinforcement schedule; they also capture the daily rhythms of feeding. Similarly, home-cage activity monitoring continuously records locomotion, which can then be analyzed alongside food-seeking behavior to uncover time-specific behavioral patterns that escape detection in traditional assays. The resulting datasets are complex, and can be mined again and again as new research questions arise. And while such rich datasets once posed analytical challenges, recent advances in analytical tools, especially those leveraging artificial intelligence, are breaking down such barriers, making sophisticated analyses accessible to all researchers, especially trainees. In sum, open-source tools are broadening access to behavioral neuroscience and enabling new lines of inquiry into feeding and motivation.

11:00

Ingestion On A Budget: Digital Mealtime Photography For Scalable Eating Behavior Assessment

Laura L Bellows

Cornell University, Ithaca, NY, United States

Measuring eating behaviors is often expensive, staff-intensive, and disconnected from real-world contexts, limiting scalability, particularly in low-resource populations. Digital food photography offers a cost-effective alternative that captures eating behaviors where they actually occur: at home. Prior work using the Remote Food Photography Method demonstrated feasibility among low-resource families, with 85% of expected dinner meal images captured and yielding rich contextual data on meal timing, preparation, and quality. Similarly, food photography in child care settings has enabled objective assessment of foods offered and consumed, revealing persistent gaps in diet quality (e.g., only 16% of packed lunches meeting nutrition guidelines) while reducing reliance on direct observation. Building on this foundation, we developed a mobile app-based mealtime photography tool that enables parents to capture before-and-after images of their child's meals in real time. This approach reduces participant burden while generating objective data on foods offered, intake, and meal quality in the home environment. Pilot data demonstrate strong feasibility and engagement with repeated photo capture, supporting its use as a scalable assessment strategy. By shifting data

collection from researchers to caregivers, digital food photography transforms assessment into a low-cost, scalable tool that can also support intervention delivery. This approach offers a practical pathway to expand access to behavioral nutrition interventions in resource-constrained settings and provides new insight into the context of eating behaviors beyond intake alone.

10:00 - 11:30 AM	Millennium Hall
Oral Session 8: Circuit City: Connections in Ingestive Behavior	

Chair(s): Marise Parent

10:00

A Homecage Social Operant Task To Investigate Diet-Induced Changes In Social Motivation

Yiru Chen, Susan E. Maloney, Alexxai V. Kravitz

Washington University in St. Louis, St. Louis, MO, United States

Obesity and high-fat diet (HFD) consumption alter reward-related neural circuits, including dopaminergic signaling, which is critical for motivated behaviors. While metabolic consequences of HFD are well characterized, less is known about how these diets influence social motivation, a key domain disrupted in several neuropsychiatric conditions. We hypothesize that chronic HFD impairs social motivation in mice through disruption of dopamine signaling. To test this, adult C57BL/6J mice (both sexes) were assessed using a homecage social operant paradigm developed in our laboratory that enabled continuous, low-stress measurement of social motivation across days. In this task, mice performed a nose-poke to open an automated door granting access to a conspecific, allowing quantification of social-seeking behavior and its circadian rhythms. Our previous work found that a social partner increased social-seeking behavior, which could be reduced by dopamine antagonists. Mice maintained on standard chow or HFD were assessed for social operant responding across the circadian cycle, while dopaminergic activity was concurrently measured using fiber photometry to determine how diet-induced changes in metabolic state affect neural encoding of social reward. This approach enabled simultaneous assessment of feeding manipulation, neural activity, and social behavior in an ethologically relevant context. These findings provide insight into how diet-induced metabolic dysfunction impacts social motivation and its neural substrates, advancing understanding of interactions between energy balance, dopamine signaling, and social behavior.

10:15

Circuit-Specific Effects Of Post-Ingestive Modulation Of Dopamine In Food Reward

Tung T Bui¹, Bhaskar Ray², Brandon Cox¹, Alec Hartle¹, Alexandria Difeliceantonio¹, Srijan Sengupta², William M Howe¹

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Post-ingestive signals triggered by gut nutrient sensors contribute to food reward in part by affecting dopamine (DA) release dynamics in the striatum. However, the spatial and temporal signatures of these post-ingestive effects, and their causal contributions to different components of food reward are less clear. Here, we conducted a series of experiments to test the hypothesis that temporally and spatially specific effects on striatal DA release enable post-ingestive signals to mediate both the attractiveness of food rewards, as well as food cue-reward learning. In the first study, we implanted intragastric (iG) catheters in C57 mice to measure the influence of post-ingestive signals triggered by different macronutrients (lipids, sucrose, combination, or PBS) on DA release in the dorsal striatum (DS, n=7) and nucleus accumbens (NAc, n=8). We found that these infusions selectively modulated the amplitude of spontaneous DA in the DS, and that this effect peaked 10-20 minutes after nutrient infusion. To assess the causal role of these effects on food choice, channelrhodopsin was expressed in the DA neurons of SNc of DAT-Cre mice (N=10). We found that amplifying DA release selectively during this time window of peak post-ingestive effects was sufficient to increase preference for a previously non-preferred macronutrient. Finally, in a separate cohort of mice (n=13) we show that post-ingestive signals triggered by iG macronutrient infusions were sufficient to support the temporal shift of DA to reward-predictive cues in the NAc, but not the DS. Our combined data support a model whereby post-ingestive modulation of DS vs NAc DA release are necessary and sufficient to support food preference, and food cue-reward learning, respectively.

10:30

Prefrontal&Ndash;Hypothalamic Dynamics During Binge-Like Eating: Feeding Microstructure And In Vivo Neural Activity During Palatable Food Consumption

Astrid Munoz-Perez de Arce¹, Pablo R. Moya^{2,3}, Ignacio Negron-Oyarzo²

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Binge eating (BE) is characterized by the rapid consumption of palatable food (PF), reflecting impaired cognitive control over feeding behavior. The lateral hypothalamus (LH) regulates consummatory processes, while the medial prefrontal cortex (mPFC) contributes to inhibitory control. However, whether mPFC-LH communication is altered during binge-like feeding behavior remains unknown. We hypothesize that binge-like feeding is associated with impaired mPFC-LH coupling during PF consumption. To test this, adult female C57BL/6 mice were subjected to intermittent access to PF for 4 weeks to induce BE. Simultaneous in vivo electrophysiological recordings (local field potentials and single-unit activity) were obtained from the mPFC and LH during feeding sessions. Binge animals exhibited a time-dependent increase in feeding bursts compared to controls (n = 7 per group, p <0.05), primarily concentrated within the first 15 minutes of the session, indicating temporally clustered intake. Preliminary analyses suggest reduced firing rates in the mPFC, but not in the LH, during PF consumption

events in binge animals at Week 4 (mPFC: 91 vs 67 units; LH: 46 vs 45 units, binge vs control; recordings from 2 animals per group), indicating region-specific alterations in neural activity. These findings indicate region-specific neural alterations associated with binge-like feeding. Ongoing analyses will determine how prefrontal–hypothalamic dynamics contribute to dysregulated feeding and loss of control, providing insight into circuit mechanisms underlying disordered eating.

10:45

Differences In The Propensity To Attribute Incentivization Of Food Cues Is Reflected In The Calcium Activity Of Anterior Insular Cortical Neurons

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A contributing factor to obesity is preoccupation with food-related stimuli often termed “food noise”. Individual variation in reactivity to food cues underlies food noise and contributes to difficulty in maintaining a healthy diet. In both humans and rodents, individual differences in the attribution of incentive salience to food cues is associated with overeating and weight gain. Specifically, some individuals incentivize food-predictive cues (sign-trackers) while others maintain incentivization of the outcome (goal-trackers). The mechanisms underlying these differences are unknown. Insular cortex (IC) is critical for forming associations between exteroceptive stimuli and interoceptive states and thus IC neural activity may explain differences in food-cue reactivity. Here, we expressed GCaMP6s in the anterior IC of rats to permit visualization of calcium activity in this neuronal population. Next, rats were trained on a Pavlovian conditioned approach paradigm for 7 days. IC photometry recordings were obtained and situated around behaviorally relevant events (i.e. cue delivery and food consumption). We found a significant day x phenotype interaction ($F(2, 14) = 3.976, p < .05$) as the neural response to the cue in sign-trackers was significantly higher than goal-trackers post-conditioning. Post-hoc analyses revealed that sign-trackers differed in their response to the cue from day 1 to day 7 ($p < .01$) while goal-trackers did not ($p = 0.93$). These data support that neural processing of cues within IC may explain phenotypic differences in cue reactivity. Future studies will determine if manipulating IC neural activity during cue presentations alters cue reactivity and whether administration of GLP-1 agonists reduce the neural response to food cues in sign-tracking rats.

11:00

A Pedunculopontine Nucleus To Ventral Tegmental Area Circuit Is Required For Dopamine Responses To Food And Associative Food-Cue Learning

Nicholas Smith¹, Ruoxi Wu¹, James Bianchi¹, Albert Yeung¹, Semus Wang¹, Michelle Awh¹, Sukya Williams¹, J. Nicholas Betley^{1,2,3}

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The modern food environment is brimming with advertisements, packaging, and contexts that powerfully drive consumption. As we associate these cues with the palatable and rewarding food that they predict, the cues themselves gain motivating power over our eating decisions. However, the neural circuits that shape associative learning for food cues are incompletely understood. We hypothesized that excitatory input to the dopamine system mediates the communication of cue and food reward information, enabling associative learning that ascribes appetitive drive to food cues. Here, we demonstrate in mice that the pedunculopontine nucleus (PPN) to ventral tegmental area (VTA) circuit is required for phasic dopamine release across the brain in both the nucleus accumbens and the basolateral amygdala. Inhibiting the PPN to VTA circuit causes significant deficits in both appetitive Pavlovian conditioning and fear conditioning, without impairments in instrumental learning or food motivation. Using endoscopic calcium imaging, we found that hunger increased the proportion of PPN cells responding to food, whereas satiety hormones suppress neural activity in the PPN. Furthermore, we identify synaptic and intrinsic electrophysiological mechanisms that support increased excitation of the PPN during hunger. Finally, we use spatial transcriptomics to parse apart genetically defined cell clusters in the PPN with distinct functional roles. Together, these findings describe the PPN to VTA circuit as essential in the neural architecture for food reward, enabling food to project dopamine across the brain and support associative learning. Therapeutically targeting this pathway could alter the motivational impact of eating and limit the ability of food cues to tempt unhealthy eating.

11:15

Lateral Hypothalamic Circuits Integrate Threat And Food Value To Drive Compulsive Eating In Obese Mice

Richard O'Connor, Paul Kenny

Icahn School of Medicine/Mount Sina, New York, NY, United States

We investigated how the hypothalamus-habenula circuit influences foraging behavior and its connection to obesity. Through in vivo calcium imaging in mice, we discovered that neurons in the lateral habenula (LHb) respond to food detection in ways shaped by the level of environmental threat. As mice gain weight, these LHb responses change, so even in hazardous situations, palatable food produces “value signals” similar to those seen during starvation. Consequently, mice with diet-induced obesity fail to adapt their feeding behavior, continuing to consume palatable food even in environments associated with aversive footshock or in the presence of an innately aversive stimulus, such as TMT. Using ex vivo electrophysiology, we found that lateral hypothalamic (LH) glutamatergic neurons projecting to the habenula were hyperpolarized in obese animals. Employing the FOS-Cre TRAP system, we selectively expressed inhibitory hM4Di DREADD in LH neurons activated by TMT exposure. Administration of the DREADD ligand CNO prevented animals from reducing food intake during subsequent exposures to TMT or environments associated with aversive footshock. We observed similar disruptions in adaptive behaviors when we directly inhibited activity in the LHb or virally lesioned excitatory input to the LHb. Thus, inhibiting threat-responsive neurons in the LH and their connections to the LHb resulted in compulsive feeding that failed to adjust to threatening stimuli. Notably, these behaviors mirrored those seen in mice that became obese after extended access to highly palatable foods. We propose that LH glutamatergic neurons, via projections to the LHb, link food value to risk tolerance, and shifts in these habenular value signals precipitate compulsive eating in obesity.

11:30 - 1:00 PM	On Own
Lunch on Own	

1:00 - 2:00 PM	Regency B
Mars Lecture 4: Corby Martin	

Chair(s): Travis Masterson
1:00

Assessment And Modification Of Ingestive Behavior As A Multi-Component Construct: Selecting The Best Method For The Population And Variable Of Interest
Corby Martin
Pennington Biomedical Research Center, Baton Rouge, , United States

Ingestive behavior is a multi-component construct encompassing several distinct behaviors and variables of interest. Various methods exist to assess ingestive behavior and these methods vary widely on their approach; assumptions; participant, researcher, or clinician burden; and incorporation of technology. Moreover, the validity of these methods varies widely, yet the validation data is not always consistent over different populations, endpoints of interest, or the state of participant (e.g., weight stable vs. weight unstable). This can result in selecting and using a dietary assessments method that is not suited for the variable of interest or the target population. These risks can be minimized, however, if we gain a better understanding of which aspect of ingestive behavior is the most relevant study or clinical outcome, and which methods are empirically supported to assess those outcomes in the population of interest. These issues will be reviewed during this talk and will include a critical review of assessing dietary and energy intake across the lifespan using a wide range of assessment methods, in addition to assessing meal frequency and meal timing via passive technology. Attendees will gain a better understanding of the strengths and weaknesses of dietary assessment methods based on what aspect of ingestive behavior is of interest and among which populations. Further, the review of assessment methods will include their ability to support modification of ingestive behaviors, including what and how much food is consumed, and when eating occurs.

2:00 - 2:50 PM	Regency B
Business Meeting	

3:00 - 4:45 PM	Regency B
Awards Session	

- P15
3:00

Kevin Williams - Hoebel Prize For Creativity, Introduction By Jeffrey Zigman
 Kevin Williams
 UT Southwestern
- P15
3:35

Amber Alhadeff - Alan N.Epstein Research Award, Introduction By Alexxai Kravitz
 Amber Alhadeff
 Monell Chemical Senses Center
- P16
4:10

Barbara Rolls - Distinguished Career Award, Introduction By Faris Zuraikat And Hanim Diktas
 Barbara Rolls
 The Pennsylvania State University

6:30 - 10:30 PM	Millennium Hall
Awards Ceremony & Closing Banquet	

The SSIB Awards Ceremony & Closing Banquet will be held in Millennium Hall in the Loews Philadelphia Hotel on level 2 from 6:30 PM to 10:30 PM.

Please bring your badge for entry, your ticket is indicated on your badge with a wine glass.

If your plans have changed and you no longer plan to attend, please visit the registration desk to let us know.