27th Annual Meeting of the Society for the Study of Ingestive Behavior

Printable Program

July 9-13, 2019
Jaarbeurs
Utrecht, NL

Tuesday, July 9, 2019

9:00 - 1:00 PM	Mission 1
Science of Behavior Change Workshop	

Bringing an Experimental Medicine Approach to the Science of Behavior Change: A Hands-on Introduction to the NIH SOBC Program Researchers world-wide are coalescing around promising approaches to advance a mechanism-focused behavior change science to address the tremendous disease burden posed by maladaptive behaviors, including overeating and unhealthy diets. Indeed, supported by the National Institutes of Health Common Fund, the Science of Behavior Change (SOBC) Program seeks to make behavior change research more impactful, targeted, and systematic by promoting a common, mechanism-focused, experimental medicine approach. In this pre-conference workshop led by members of the SOBC Program and other like-minded researchers from around the globe, attendees will be introduced to SOBC and learn about insights, initial findings, and resources from this initiative. Attendees will also get firsthand experience with the SOBC method and resources by applying them to their own research interests. In addition, workshop participants will engage in interactive discussions about the challenges, opportunities, and next steps in the area of behavior change science, particularly as it intersects with the interests and priorities of the Society for the Science of Ingestive Behavior.

Chair(s): Luke Stoeckel, Jeffrey Birk, Jun Ma, Anne Roefs and Anita Jansen

10:00 - 12:00 PM	Offsite NH Hotel
SSIB Board Meeting (Invitation Only)	

4:45 - 5:00 PM	Progress
Opening Greetings	

5:00 - 6:00 PM	Progress
MARS LECTURE 1	

Chair(s): Alain Dagher

5:00 **The Genetics Of Obesity -** ***From Genes To Biology &Hellip; To Clinical Practice***
RUTH J.F. LOOS
Icahn School of Medicine at Mount Sinai, New York, NY, United States

Obesity is a major chronic disease, posing an enormous burden on people's health. While a major driver of the current epidemic is undoubtedly our changing environment, people's genetic predisposition will determine the extent to which they respond to the obesogenic lifestyle. Indeed, twin and family studies have estimated that 40-70% of the inter-individual variation in obesity susceptibility is due to genetic variations. Since the discovery of the *FTO* locus in 2017, genome-wide association studies have reported more than 1,000 genetic loci associated with body mass index, obesity and other adiposity traits. While their explained variance is a small, tissue enrichment and pathway analyses for genes within obesity-associated loci have repeatedly shown that the central nervous system plays a critical role in body weight regulation, likely through control of regulatory and hedonic aspects of food intake. A major challenge, however, remains pinpointing the causal gene within each genetic locus, a critical step towards translation of GWAS-discoveries into functional experiments. So far, a few successful fine-mapping efforts have revealed genes not previously presumed to be implicated in obesity. More recent genome-wide studies have focused on rare, coding variants, that affect protein function. Despite enormous sample sizes, few such variants have been identified, but their effects are larger and have pointed to new candidate genes, and thus new biology. With increasing number of discoveries, it has been speculated that genetic variants can soon be used to predict future obesity. However, current results suggest that prediction solely based on genetic variation will not be accurate, even not for functional mutations, and that other factors, such as family history, are more predictive.

6:00 - 8:00 PM	Transit Zone
OPENING RECEPTION	

8:00 - 9:00 PM	Offsite - Brasserie Domplein
New Investigator Event	

Wednesday, July 10, 2019

8:30 - 10:30 AM	Progress
NITA SYMPOSIUM	

Chair(s): Derek Daniels

8:30 **Using *In Vivo* Two-Photon Fluorescence Endomicroscopy To Measure Activity Of Lateral Hypothalamic Glutamatergic And Gabaergic Neurons In Response To Sugar Consumption In Mice Fed A Free Choice High-Fat Diet.**

LAURA L. KOEKKOEK[1, 2], MARGO SLOMP[1, 2], SARAH SARSFIELD[3], MICHAEL MUTERSBAUGH[3], IAN LINVILLE[3], MIREILLE J. SERLIE[1], YEKA APONTE[3], SUSANNE E. LA FLEUR[1,2]

[1]Department of Endocrinology & Metabolism, Academic Medical Center, Amsterdam, Netherlands, [2]Metabolism and Reward Group, Royal Netherlands Academy of Arts and Sciences, Netherlands Institute of Neuroscience, Amsterdam, Netherlands, [3]Intramural Research Program, Neuronal Circuits and Behavior Unit, National Institute on Drug Abuse, Baltimore, MD, United States

The lateral hypothalamus (LH) is crucial for regulating appetitive and consummatory behaviors. While it is known that overconsumption of high fat-sugary foods can lead to obesity, the precise mechanisms and circuits underlying these behaviors have yet to be determined. Inhibition of glutamatergic LH neurons results in preference for palatable foods, whereas stimulation of GABAergic LH neurons increases palatable food intake. As our previous studies show that co-occurring consumption of fat and sugar induces hyperphagia, we hypothesized that sugar consumption after free-choice high-fat diet (fcHFD) feeding reduces excitatory output from the LH. Using *in vivo* two-photon microscopy, we analyzed activity changes in glutamatergic or GABAergic LH neurons in control diet (CD)- or fcHFD-fed mice in response to water or sugar drinking. We observed that the percentage of GABAergic neurons that increase their activity in response to sugar is significantly higher in CD-fed mice versus fcHFD-fed mice (19.54% vs. 11.41%, $p< 0.05$)). In glutamatergic neurons, this percentage was significantly lower in CD-fed mice compared to fcHFD-fed mice (15.11% vs. 20.85%, $p< 0.05$). Moreover, when glutamatergic neurons increased their activity in response to sugar, they did so to a larger degree in fcHFD-fed mice than neurons in the CD-fed mice on the second (AUC of 20.07 vs. 11.70, $p< 0.05$) and third day (AUC of 14.71 vs. 9.71, $p< 0.05$) of sucrose consumption. In the present study, we show an interacting effect of fat and sugar consumption on GABA-ergic and glutamatergic neuronal activity. Interestingly, the net result of this interacting effect is an increase in excitatory output, and therefore further research is needed to unravel how this contributes to the development of hyperphagia.

8:45 **Hippocampus Ghrelin Signaling Increases Meal Size Through A Descending Hypothalamic To Hindbrain Signaling Pathway**

ANDREA N SUAREZ[1], CLARISSA M LIU[2], ALYSSA M CORTELLA[1], EMILY E NOBLE[1], SCOTT E KANOSKI[1,2]

[1]Department of Biological Sciences, University of Southern California, Los Angeles, CA, United States, [2]Neuroscience Graduate Program, University of Southern California, Los Angeles, CA, United States

In addition to classic hindbrain substrates, emerging findings reveal that meal size control is also influenced by processing in higher-order brain regions. One such region is the hippocampus, which is historically associated with learning and memory control and more recently with feeding-related cognitive processes. Here we reveal in rats that the gut-derived hormone ghrelin acts in the ventral hippocampus (vHPC) to increase food intake via an increase spontaneous meal size. To identify underlying mechanisms, additional results show that a dose of vHPC ghrelin that is subthreshold for feeding effects alone attenuates the anorectic effects of vagally-mediated satiation signals, including peripheral administration of cholesystokinin and following gastric distension by methylcellulose gavage. Next to determine the downstream neural pathways, we utilized a transsynaptic virus-based tracing strategy to identify a multi-order connection from the vHPC to the laterodorsal tegmental nucleus (LDTg) in the hindbrain. Further, neurons in the lateral hypothalamic area (LHA) that produce the neuropeptide orexin (aka, hypocretin) were identified as a relay connecting the vHPC to the LDTg. To determine the functional relevance of this pathway to satiation control, we next investigated whether vHPC ghrelin signaling increases spontaneous meal size via downstream LHA orexin signaling to the LDTg. Results show that pharmacological orexin 1A receptor blockade in the LDTg attenuates vHPC ghrelin-mediated elevations in meal size. We conclude that vHPC ghrelin signaling increases meal size through interactions with gut-derived vagally-mediated satiation signals, and that these effects may occur through a descending pathway connecting the vHPC to the hindbrain LDTg via LHA orexin signaling.

9:00 **(Collier Award Winner) Distraction-Induced Decreases In Brain Responses Relate To Continued Effort For Food Reward After Satiation**

IRIS DUIF[1], JOOST B. WEGMAN[1], PAUL A. SMEETS[2], CEES DE GRAAF[2], ESTHER AARTS[1]
[1]Radboud University, Nijmegen, Netherlands, [2]Wageningen University, Wageningen, Netherlands

Distracted eating is associated with increased food intake. However, little is known about the underlying neural mechanisms. We hypothesized (for the preregistration of this study, see: https://osf.io/k998e/?view_only=ae19c2bb78ac4b59a69669a5b129cab8) that distraction attenuates satiation-sensitive, i.e. outcome-sensitive, responses towards food rewards. We expected this attenuation to be associated with decreased responses in the ventromedial prefrontal cortex (vmPFC) or other fronto-striatal regions. Thirty-eight healthy, normal-weight participants performed a visual detection task varying in attentional load (high or low distraction) during fMRI. Simultaneously, participants exerted effort for food reward by repeated button presses for two types of snacks (sweet or savoury). Reward outcome sensitivity was assessed by comparing effort before versus after outcome devaluation by sensory-specific satiation. There was no effect of distraction on effort for food reward as a function of satiation. Neurally, distraction tended to affect satiation-related responses in the right inferior frontal gyrus (rIFG, $p < .001$, uncorrected) rather than the vmPFC. Importantly, these distraction-sensitive rIFG responses for valued versus devalued food rewards significantly correlated with the same effect in the number of button presses ($r=-.40$, $p=.014$). Specifically, distraction-related rIFG decreases were associated with continued button presses for food reward after satiation, in line with rIFG's established role in response inhibition. Our results suggest that distraction attenuates the ability to inhibit responses for food reward after satiation by acting on the rIFG. This reduction in outcome-sensitive responses towards food reward might explain why distraction can lead to overeating.

9:15 **High Dietary Restraint Is Associated With Increased Performance On A Food Motivated Probabilistic Selection Task And Visual Cortex Response To Punishment Via Taste.**

JENNIFER R SADLER, GRACE E SHEARRER, NICOLLETTE T ACOSTA, KYLE S BURGER
University of North Carolina at Chapel Hill, Chapel Hill, NC, United States

Reinforcement learning informs choices that aim to maximize reward and minimize punishment. High dietary restraint (DR) is related to deficits in flavor-reinforcer learning. The relation between DR and reinforcement learning is limited to passive conditioning tasks. Here, we tested the relationship between DR and food reinforcement using an instrumental conditioning task with gustatory feedback. We hypothesized high DR would relate to impaired performance during the task. 90 adults (57%F, age:21.6±2.3y, BMI:24.5±3.3) completed DEBQ Restraint scale, N-Back task, and fMRI probabilistic selection task (PST). In the PST-training, participants learn to select a shape from pairs via probabilistic feedback from calorically-matched tastes: sweet (reward) or bitter (punishment). In the PST-test, reward and punishment learning is tested without further reinforcement. DR groups were selected by tertiles: High DR (n=29, >2.5) and low DR (n=30, < 1.8). High DR was associated with significantly higher BMI ($t=3.2$, $p=0.003$) and lower N-back accuracy ($t=2.1$, $p=0.045$) vs low DR. In the PST-test, the high DR group had more "learners" (chose the rewarded shape and avoided the punished shape) than the low DR group, trending significant ($X^2=7.2$, $p=0.07$). In PST-training, high DR was associated with significantly greater brain response in the inferior visual cortex (k=25, peak MNI:15, -69, 12, z=4.0) to bitter>neutral taste. Here, we found high DR was related to higher BMI and decreased working memory performance compared to low DR. We found that high DR was associated with improved performance on a gustatory instrumental conditioning task. This may be mediated by brain response during punishment in the visual cortex, which is implicated in short term memory consolidation.

9:30 **Leucine Sensing In The Caudomedial Hindbrain Rapidly Inhibits Agrp Neurons**

ANTHONY H TSANG, DANAE NUZZACI, TAMANA DARWISH, EMMA ROTH, HAVISH SAMUDRALA, CLEMENCE BLOUET
MRC Metabolic Diseases Unit, University of Cambridge Metabolic Research Laboratories, WT-MRC Institute of Metabolic Science, University of Cambridge, Cambridge, United Kingdom

Among all macronutrients, protein has the most potent appetite-suppressing effect. However, how protein availability is encoded and detected by the brain to modulate behaviour is unclear. We propose that circulating leucine levels serve as a postprandial signal of protein availability. We previously showed that leucine sensing in the the dorso-vagal complex (DVC) rapidly suppresses hunger, but the neural circuits mediating this response are unknown. Here we used a combination of viral tracing studies and histological assessments to characterise the central pathways engaged downstream from DVC leucine sensing to rapidly suppress hunger. First, we showed that DVC leucine sensing can rapidly inhibit AgRP neurons ($AgRP^{ARC}$) in fasted mice. We found that $AgRP^{ARC}$ neurons receive poly-synaptic inputs from two distinct subpopulations of catecholamine neurons in the DVC expressing either calcitonin receptor (CTR) and prolactin-releasing peptide (PrRP), and found that DVC leucine sensing activates these two neuronal subsets. We deciphered the neural pathways through which DVC interception modulates the activity of AgRP neurons via relays in the dorsomedial and paraventricular nuclei of the hypothalamus. Last we confirmed the functional relevance of the DVC - $AgRP^{ARC}$ circuit in the regulation of feeding behaviour. Together, these findings shed light in elucidating the central leucine-sensing mechanism and describe a novel neural pathways through which hindbrain nutrient sensing is relayed to key appetite-regulating neurons of the hypothalamus.

9:45 **(Sakai Award Winner) The Subfornical Organ Recruits Phasic Dopamine Signalling To Water Availability Via Multi-Order Pathways**

TM HSU, VR KONANUR, P BAZZINO, MF ROITMAN
University of Illinois at Chicago, Chicago, IL, United States

Changes in physiological state, including hunger, satiety, and body fluid homeostasis, can strongly modulate

phasic dopamine signalling and goal-directed behaviors. Here we examine the novel hypothesis that the subfornical organ (SFO), a key central thirst detector, relays need state information to mesolimbic dopamine pathways to regulate thirst-motivated behaviors. To capture phasic dopamine dynamics, we utilized in vivo fiber photometry in rats that express protein-based fluorescent sensors to measure ventral tegmental area (VTA) dopamine neuron activity (Cre-dependent gCaMP6f in TH-Cre+ rats) or dopamine release (dLight1.2) in the nucleus accumbens shell (NAc shell). In water-restricted rats allowed intermittent, cued sipper access, we first demonstrated that VTA dopamine neuron activity and NAc shell dopamine release develop to cues associated with water. After training under water-restriction, we find a lack of cue-evoked VTA and NAc phasic dopamine activity when rats are water-sated. SFO glutamatergic neurons (SFO^{glu}) are engaged during thirsty states and selective activation of SFO^{glu} neurons engages robust water intake in water-sated animals. We found that DREADDs mediated activation of SFO^{glu} neurons mimics thirst in recruiting phasic dopamine activity, as SFO^{glu} activation increases water-cue evoked VTA dopamine responses. To identify potential relay nodes, we find that activation of SFO^{glu} increases c-fos expression not only in the VTA and NAc, but also the lateral hypothalamus (LH). Preliminary tract-tracing experiments further support the LH as a relay region between the SFO and VTA dopamine neurons. Overall, our findings reveal that thirst powerfully influences phasic dopamine signalling and that this occurs via multi-order SFO to VTA pathways.

10:00 **Temporal Dynamics Of Taste And Health Differ By Child Weight Status During A Food Decision Making Task**

ALAINA L PEARCE[1], SHANA ADISE[1], NICOLE J. ROBERTS[2], CHARLES F. GEIER[2], COREY N. WHITE[3], KATHLEEN L. KELLER[1,4]

[1]Nutritional Science, Pennsylvania State University, State College, PA, United States, [2]Human Development and Family Sciences, Pennsylvania State University, State College, PA, United States, [3]Psychology, Syracuse University, Syracuse, NY, United States, [4]Food Sciences, Pennsylvania State University, State College, PA, United States

Understanding how taste and health influence food choice is critical to prevention of pediatric obesity. Computer mouse tracking tasks have shown the speed at which taste and health influence choice is a marker of dietary self-control. In children, these tasks indicate more cognitive effort is needed to reject unhealthy than healthy foods. However, it remains unclear how children make decisions between foods that vary by taste and health (healthy/not tasty paired with unhealthy/tasty), a scenario more similar to real-world self-control. 67 children (7-11years; n=33 overweight/obesity-OB; n=34 normal weight-NW) completed a mouse tracking food choice task to assess dietary self-control. After rating food images for taste and health, children were presented with food pairs that were “mismatched” according to their own ratings (healthy/not tasty paired with unhealthy/tasty). For each pair, children were asked to consider health when choosing the food they wanted to eat and told that one of their choices would be served later. Healthy foods were chosen 51% of the time with no difference by weight status. As foods were “mismatched” for taste and health, the timing of when these attributes influenced decisions could be tested. A group (OB, NW) x choice (healthy, unhealthy) interaction was seen for the speed at which taste but not health impacted decision making. When choosing healthy foods, OB children took longer to discount taste, suggesting this choice took more cognitive effort than for NW children. However, groups did not differ when choosing unhealthy foods. These results highlight differences in the speed at which taste and health influence food decisions which have implications for development of child interventions to promote healthy eating.

10:15 **Coordinated, Bidirectional Modulation Of Hypothalamic Hunger And Midbrain Reward Circuits**

NITSAN GOLDSTEIN, AMBER L. ALHADEFF, ONYOO PARK, J. NICHOLAS BETLEY
University of Pennsylvania, Philadelphia, PA, United States

Motivated behavior is influenced by coordinated activity in neural circuits that integrate physiological needs. Hunger potentiates the reward value of both food and drugs of abuse, yet the underlying neural circuitry mediating this relationship is unknown. Since hypothalamic agouti-related protein (AgRP)-expressing neurons are activated by food deprivation, we tested the hypothesis that AgRP neuron activity will potentiate dopamine signaling in response to food and drugs. We used Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) to activate AgRP neurons while measuring dopamine signaling in the nucleus accumbens (NAc) using a genetically encoded dopamine sensor. Activating AgRP neurons in *ad libitum*-fed mice potentiated the dopamine responses to both food and drug rewards. In the absence of reward, AgRP neuron activation did not affect dopamine levels. We next examined whether the relationship between AgRP neuron activity and dopamine signaling is bidirectional by modulating dopamine signaling while monitoring AgRP neuron calcium dynamics using the calcium indicator GCaMP6s. Simultaneous administration of D1 and D2 receptor antagonists, at doses that did not affect AgRP neuron activity alone, attenuated AgRP neuron responses to natural and drug rewards. Taken together, these results suggest that an interconnected circuitry exists between hypothalamic AgRP neurons and midbrain dopamine neurons that may underlie the coordinated regulation of motivated behavior by homeostatic and hedonic circuits.

10:30 - 11:00 AM	Transit Zone
Coffee Break	

11:00 - 12:00 PM	Progress
MARS LECTURE 2	

Chair(s): Matt Hayes

11:00 **Targeting Brain Serotonin 2C Receptors To Improve Obesity**
LORA K HEISLER
Rowett Institute, University of Aberdeen, Aberdeen, United Kingdom

Obesity has become one of the major health concerns of this century because of its prevalence and resistance to treatment. Significant progress has been made over the past decade in clarifying brain neurochemicals and regions regulating energy homeostasis. Among these is the key precursor polypeptide pro-opiomelanocortin(Pomc). In the brain, Pomc is expressed within the homeostatic brain regions the arcuate nucleus of the hypothalamus (ARC) and the nucleus of the solitary tract (NTS). The 5-hydroxytryptamine (5-HT, serotonin) 2C receptor (*Htr2c*; 5-HT_{2C}R) agonist lorcaserin (Eisai, Inc) is a medication for obesity treatment that was recently launched in the USA. However, mechanism through which lorcaserin's therapeutic effects are achieved remain to be elucidated. Here we clarify that a target of lorcaserin is 5-HT_{2C}Rs influencing the activity of ARC and NTS Pomc. Specifically, here we demonstrate that preventing Pomc production in the ARC ($Pomc^{NEO}$) is sufficient to abolish lorcaserin's anorectic effects and that restoration of *Pomc* specifically within a subset of ARC neurons expressing 5-HT_{2C}Rs ($Pomc^{Htr2c}$) is sufficient to restore lorcaserin's therapeutic effect. Further, we demonstrate that knocking down Pomc specifically within the NTS prevents the full effect of lorcaserin to suppress food intake. These findings illustrate that lorcaserin achieves it therapeutic benefit via activation of ARC and NTS Pomc. These findings thereby reveal a necessary mechanism underpinning the therapeutic benefit of the new obesity medication lorcaserin, via activation of brain Pomc.

12:00 - 4:00 PM	Lunch On Own
LUNCH	

1:30 - 3:30 PM	Mission 1
Open Source Resources in Ingestive Behavior	

Lex Kravitz will present some recent developments in open-source hardware for ingestive and behavioral research. He will highlight a few open-source devices and discuss the advantages of these devices in research studies. Finally, he will lead the audience through an interactive example to demonstrate how open-source devices can be built and used without advanced knowledge of electronics or coding. Lack of reproducible research is a major threat to the advancement of ingestive behavior research. Kyle Burger will present some of the concerning scientific approaches that perpetuate non-reproducible results followed by a discussion on simple scientific practices that serve to increase the rigor and transparency of ingestive behavior research. Lastly, he will provide a demonstration of some of the tools (e.g., NutrXiv, a preprint service; Open Science Framework) available that facilitate rigorous and rapidly accessible research. The Core Neuropsychological Measures for Obesity and Diabetes Trials Project aimed to (1) identify the key cognitive and perceptual domains in which performance can influence treatment outcomes, including predicting, mediating, and moderating treatment outcome and (2) to generate neuropsychological batteries comprised of freely available and easy-to-administer tests that best measure these key domains. The ultimate goals of this project are for the batteries to be used in ongoing and future obesity and diabetes trials so that the relationship between cognition and obesity and diabetes can be better understood, in turn identifying the most promising cognitive domains as targets for intervention. Luke Stoeckel and Dana Small will present the rationale for the project and three options for the neuropsychological batteries to satisfy varying time and other administration constraints.

Chair(s): Lex Kravitz, Kyle Burger and Luke Stoeckel

4:00 - 6:00 PM	Progress
SYMPOSIUM 1: From Genes to Therapy	

Chair(s): Tony Goldstone and Uku Vainik

4:00 **Preclinical Testing In Animal Models Of Prader-Willi Syndrome: From Genes To Therapy**
RACHEL WEVRICK, JOCELYN M BISCHOF, KARIN V CARIAS, MATTHEA R SANDERSON
Medical Genetics, University of Alberta, Edmonton, AB, Canada

Prader-Willi syndrome (PWS) is a rare genetic form of hyperphagia leading to severe obesity, and is caused by

the inactivation of contiguous genes on chromosome 15q1-q13. People with PWS also have endocrine, musculoskeletal, and neurological dysfunction. Loss of function of several genes, including MKRN3, MAGEL2, NDN, SNORD116 and IPW have been proposed to contribute to PWS phenotypes. Mice with gene-targeted mutations in one or more of these PWS genes recapitulate some PWS-like symptoms, and can be used to measure the effect of therapeutics. Indeed, seven categories of therapeutics (oxytocin and related compounds, K+-ATP channel agonists, melanocortin 4 receptor agonists, incretin mimetics / GLP-1 receptor agonists, cannabinoids, ghrelin agents, and Caralluma fimbriata (cactus) extract) have been tested for their effects in both PWS animal models and clinical trials. In addition to evaluating to possible effectiveness of a therapeutic for the treatment of PWS, animal models can be used to elucidate the deficiencies in appetitive and energy balance pathways that lead to hyperphagia and obesity in PWS. Strategies to accelerate the discovery and translation of therapies into clinical practice in PWS will be discussed.

4:30 **New Therapies For Patients With Leptin/Melanocortin Deficiency**
KARINE CLEMENT, CHRISTINE POITOU, BÉATRICE DUBERN
Sorbonne Université/ INSERM NutriOmics research group, Paris, France

5:00 **The Nature Of Nurture: Gene-Environment Interplay In The Development Of Eating Behaviour And Adiposity**
CLARE H LLEWELLYN
University College London, London, United Kingdom

Despite the ubiquity of the modern ‘obesogenic’ environment, we have not uniformly developed obesity. On the contrary, there is considerable variation in weight gain, which is observable from early infancy. In fact, it is not uncommon for siblings to vary considerably in their weight, even when they live in the same household. Obesity risk is about far more than just the environment we are exposed to. Genetic susceptibility to the environment is thought to explain some of the variation in adiposity. Nearly 100 twin studies have established that weight is a highly heritable trait (50-90%), and >700 common genetic variants have been discovered. Individual differences in appetite have been implicated as one of the mechanisms through which genes influence adiposity, so-called ‘Behavioural Susceptibility Theory’ (BST). BST hypothesises that individuals who inherit a set of genes that confer greater responsiveness to food cues (wanting to eat in response to the sight, smell or taste of palatable food), and lower sensitivity to satiety (fullness), are more vulnerable to overeating in response to the modern food environment, and therefore to developing obesity. At the same time, our environment is not simpy an ‘exposure’ – we select and shape our environment to suit our preferences, many of which have some genetic basis (called gene-environment correlation). This talk summarises the interplay between genes, appetite and the home family environment in early weight gain, using data from Gemini and TEDS – two large, population-based British twin birth cohorts set up to study genetic and environmental influence on development.

5:30 **A High Sugar Diet Reshapes Sweet Taste And Promotes Feeding Behavior In *Drosophila***
CHRISTINA MAY, ANOUMID VAZIRI, MONICA DUS
Department of Molecular, Cellular, and Developmental Biology, The University of Michigan, Ann Arbor, MI, United States

The sensation of pleasurable food qualities such as sweetness plays a crucial role in regulating feeding. Recent studies found that humans with obesity have lower taste responses to sweet stimuli. Whether these sensory changes are a metabolic consequence of obesity, or occur because of exposure to specific diets is unclear. Furthermore, their role in the etiology of obesity is unknown. To understand how changes in sweet taste occur and what impact they have on feeding patterns, we studied the effects of a high sugar diet on sweet taste sensation in *Drosophila melanogaster*. Feeding fruit flies a high sugar diet resulted in decreased sweet taste sensation because of lower responses of the sweet taste cells to sugar stimuli. By using genetically obese and lean animals, we found that high dietary sugar, not obesity or dietary sweetness, promoted taste deficits through the cell-autonomous action of the conserved sugar sensor *O-GlcNAc Transferase* in the sweet sensory neurons. By monitoring feeding behavior at high resolution and using opto- and neurogenetics manipulations of sweet taste cell activity, we show the dulling of sweet taste leads to overfeeding and obesity. Preventing a decrease in sweet taste sensation rescues feeding and fat accumulation in animals exposed to the high sugar diet. Our work demonstrates that the reshaping of sweet taste sensation by high dietary sugar is a driver of obesity and highlights the role of metabolism in altering neural activity and behavior.

4:00 - 6:00 PM	Mission 1
ORAL SESSION 1: Feeding Circuits in Humans and Animal Models	

Chair(s): Amber Alhadeff and Matt Carter

4:00 **Hippocampus-Lateral Septum Circuitry Regulates Memory For The Spatial Location Of Food**

CLARISSA M LIU[1,2], ELIZABETH A DAVIS[1], ANDREA N SUAREZ[1], EMILY E NOBLE[1], SCOTT E KANOSKI[1,2]

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

While foraging is an essential behavior for survival, surprisingly little is understood about its underlying neural substrates. The hippocampus is strongly associated with memory based on visuospatial information, a key component of foraging behavior. However, the overwhelming majority of research on the hippocampus and spatial memory has utilized procedures that require escaping aversive stimuli in the environment, whereas very little is known about its role in memory for the spatial location of food. The present study examined whether the ventral hippocampus (vHPC), a region recently associated with conditioned aspects of feeding behavior, plays a role in learning and remembering the spatial location of food. Results reveal that excitotoxic lesions of the vHPC in rats impair memory retention, but not learning, in a newly developed spatial food-seeking rodent behavioral task. We hypothesized that the lateral septum (LS) is a possible downstream target mediating vHPC-mediated spatial food memory, as our additional tract tracing analyses identify the LS as a primary output of the vHPC CA1 subregion (vCA1). To examine this hypothesis, we utilized conditional dual viral approaches to either reversibly (via cre-dependent pathway-specific inhibitory chemogenetics) or permanently (via cre-dependent pathway-specific caspase-induced lesions) disconnect vCA1 to LS communication. Results show that both acute and chronic disruption of vCA1 to LS signaling impairs memory retention, but not learning, in the spatial food seeking task. Collectively these data indicate that vHPC communication to the LS plays an important role in memory for food-related environmental cues, and thus we've identified a novel neural pathway that may be critical for foraging-related learning and memory.

4:15 **Uncovering The Spatial Representation Of Taste Identity In The Human Brain**

JASON A. AVERY, STEPHEN J. GOTTS, JOHN E. INGEHOLM, CAMERON D. RIDDELL, ALEXANDER G. LIU, ALEX MARTIN
Laboratory of Brain and Cognition, National Institute of Mental Health, Bethesda, MD, United States

In the mammalian brain, the insula is the primary cortical substrate involved in taste perception. Recent imaging studies in rodents have identified a 'gustotopic' organization in the insula, whereby distinct insula regions are selectively responsive to one of the five basic tastes. However, numerous studies in monkeys have reported that gustatory cortical neurons are broadly-tuned to multiple tastes, and tastes are not represented in discrete spatial locations. Neuroimaging studies in humans have thus far been unable to discern between these two models, though this may due to the relatively low spatial resolution employed in taste studies to date. In the present study, we examined the spatial representation of taste within the human brain using ultra-high resolution functional magnetic resonance imaging (MRI) at high magnetic field strength (7-Tesla). During scanning, participants tasted sweet, salty, sour and tasteless liquids, delivered via a custom-built MRI-compatible tastant-delivery system. Our univariate analyses revealed that all tastes (vs. tasteless) activated primary taste cortex within the dorsal mid-insula, but no brain region exhibited a consistent preference for any individual taste. However, our multivariate searchlight analyses were able to reliably decode the identity of distinct tastes specifically within those mid-insula regions. Beyond the insula, we were also able to decode taste identity within brain regions involved in affect and reward, such as the ventral striatum, orbitofrontal cortex, and bilateral amygdala. These results suggest that taste identity is not represented topographically, but by a distributed spatial code, both within primary taste cortex as well as regions involved in processing the hedonic and aversive properties of taste.

4:30 **(Nita Award Winner) A Central Mechanism For Individual Sensitivity To Taste**

MICHAEL C. FARRUGGIA, MARIA G. VELDHUIZEN, XIAO GAO, YUKO NAKAMURA, BARRY GREEN, DUSTIN SCHEINOST, DANA SMALL
Yale University, New Haven, CT, United States

Taste perception provides information about the nutritive and toxic potential of foods, with taste intensity acting as a reliable signal of quantity. It is therefore surprising that there are large differences in taste intensity perception across individuals. Within an individual, however, taste intensity ratings are highly correlated across tastes, pointing to a central source of variation. Removal of the anterior medial temporal lobe (AMTL) in humans undergoing surgical treatment for epilepsy results in increased sensitivity to taste, raising the possibility that an inhibitory signal from the AMTL acts as a "central gain mechanism" by gating afferent sensory signals. We tested this hypothesis using psychophysics and fMRI in 27 healthy adults. Replicating prior work, we found that intensity ratings for sweet, sour, and salty tastes were strongly correlated ($r>0.7$), with weaker correlations for bitter ($r\leq0.42$). Two types of predictive modeling employing leave-one-out cross-validation were then used to predict average intensity ratings for the three correlated tastes. Dynamic Causal Modeling, which is based on a strong *a priori* model, revealed that an inhibitory signal from the amygdala (part of AMTL) to thalamus captured 21% of variance in intensity ratings. Connectome-based Predictive Modeling (CPM), which is data driven and based on whole brain connectivity, isolated a trend towards a significant CPM ($r=0.33$, $p< 0.07$) involving bilateral thalamic and AMTL nodes of connectivity. Significant CPMs for sweet ($r=0.40$, $p< 0.05$) and sour

(r=0.40, p< 0.05) alone were also identified. These findings converge to support the existence of a central source for variation in taste intensity perception involving the thalamus and AMTL.

4:45 **A Lateral Parabrachium-Projecting Subpopulation Of Preproglucagon Neurons Encodes Meal Termination**

DANIEL I. BRIERLEY[1], IMAN SELIM[1], PAULA BARBURAS[1], FRANK REIMANN[2], FIONA M. GRIBBLE[2], STEFAN TRAPP[1]

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Preproglucagon (PPG) neurons in the nucleus tractus solitarii (NTS) produce GLP-1, and their chemogenetic activation induces a large, sustained anorectic effect. However, chemogenetic inhibition or ablation of these neurons does not affect *ad libitum* intake, but delays termination of abnormally large meals induced by fast/refeeding or palatable diet. This discrepancy may reflect a neuroarchitecture of discrete subpopulations of PPG neurons characterised by distinct projection targets, which are selectively recruited under specific physiological conditions, such as abnormally large intakes. We hypothesised that PPG neurons projecting to the lateral parabrachial nucleus (lPBN) may represent a subpopulation mediating large-meal satiation, given the known role of this nucleus in meal termination. We investigated this putative $PPG^{NTS \rightarrow lPBN}$ subpopulation first using a triple-transgenic mouse (Glu-YFP x GLP-1R-Cre:tdRFP) to show that YFP+ PPG varicose axons terminate in the lPBN, in close apposition to tdRFP+ GLP-1R-expressing neurons. We then determined that PPG neurons projecting to the lPBN are indeed a *bona fide* discrete, functionally-relevant subpopulation using a retrograde AAV (rAAV2-retro) encoding Cre-dependent hM3Dq:mCherry injected into the lPBN of mice expressing Cre-recombinase and GFP in PPGs. This selectively transduced a minority (~35%) of PPGs, which were not bifurcated or collateralised to other brain regions innervated by PPG neurons. Chemogenetic activation of this subpopulation in 18hr fasted mice was sufficient to reduce chow intake in dark phase hour 1 (by 48%; p=0.030) predominantly by decreasing meal 1 size (by 63%; p=0.022). This $PPG^{NTS \rightarrow lPBN}$ subpopulation may thus comprise part of a meal termination circuit independent of the wider brain GLP-1 system.

5:00 **Endogenous Amylin Contributes To The Birth Of Microglial Cells In The Arcuate Nucleus Of The Hypothalamus And The Area Postrema During Embryogenesis**

CHRISTELLE LE FOLL, THOMAS A. LUTZ
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Amylin acts in the area postrema (AP) and arcuate nucleus (ARC) to control food intake. Amylin also increases axonal fiber outgrowth from the AP→nucleus tractus solitarius (NTS) and from ARC→ hypothalamic paraventricular nucleus (PVN). More recently exogenous amylin infusion for 4 weeks was shown to increase neurogenesis in adult rats in the AP. Furthermore, amylin has been shown to enhance leptin signalling in the ARC and ventromedial hypothalamus (VMN). Thus, we hypothesized that endogenous amylin could be a critical factor in regulating cell birth in the ARC and AP and that amylin could also be involved in the birth of leptin-sensitive neurons. $Amylin^{+/-}$dams were injected with BrdU at embryonic day 12 and at post-natal (P) day 2, BrdU+ cells were quantified in WT and amylin KO mice. The number of BrdU+HuC/D+ neurons was similar in ARC and AP but the number of BrdU+Iba1+ microglia was significantly decreased in both nuclei. Five-week-old WT and KO littermates were injected with leptin to test whether amylin is involved in the birth of leptin sensitive neurons. While there was no difference in the number of BrdU+c-Fos+ neurons in the ARC and DMN, an increase in BrdU+c-Fos+ neurons was seen in VMN and LH in amylin KO mice. In conclusion, these data suggest that endogenous amylin favours the birth of microglial cells in the ARC and AP and that it decreases the birth of leptin-sensitive neurons in the VMN and LH.

5:15 **Altered Brain Modularity Across Body Mass Index And Pubertal Status In Adolescents**

GRACE E SHEARRER, JENNIFER R SADLER, KYLE S BURGER
University of North Carolina, Chapel Hill, NC, United States

The impact of BMI and puberty on brain development is unknown. Here, we tested whether weight and puberty status was related to integration of the cingulo-opercular (CO) brain network in adolescents drawn from the ACBD fMRI study. 120 subjects were included in the analysis (F:57; obese:41, overweight:35; mid-pubertal:41, late pubertal:44) with an average fMRI scan time of 18 min. Pubertal status was calculated from the Puberty Development Scale, and BMI categories (via BMI percentiles) were used. Regions of interest (ROIs) from the 264-Power Atlas were parceled into graphs; generated from correlation matrices per BMI group and pubertal group. Modularity (closely connected ROI groups) was determined using the Louvain algorithm. Participation coefficient (PC) was calculated to assess connectivity within/between modules and tested via ANOVAs. Unlike the healthy weight and overweight graphs with 6 modules, the obese graph produced only 5 modules. The obese group also showed decreased PC and therefore decreased connectivity between sensorimotor and cingulo-opercular networks in the obese compared to healthy weight group (pFDR< 0.01). The early and mid-pubertal groups showed 6 unique modules, whereas the late pubertal group showed 5. Across all modules the mid-pubertal group showed increased PC (between network connectivity) compared to both other pubertal groups (pFDR< 0.01). The CO network appears to be interrupted with high BMI, possibly underlying aberrant self-control. Mid-puberty shows higher connectivity between brain networks, before condensing networks in late puberty.

5:30 **Investigating Medial Amygdala Circuits In Feeding And Glucose Homeostasis**

KAVYA DEVARAKONDA[1,2], MITCHELL BAYNE[1], KAETLYN CONNER[1], DARLINE GARIBAY[1], ALEXANDRA ALVARSSON[1], PAUL J KENNY[2], SARAH A STANLEY[1,2]

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Nearly two-thirds of U.S. adults are overweight or obese, putting them at risk for other serious medical conditions, including diabetes and heart disease, but the etiology of obesity and metabolic syndrome in humans is not well understood. Delineating how the brain regulates metabolism, including feeding behavior and glucose homeostasis, may shed light on how those processes are altered in disease. The medial amygdalar nucleus (MeA) regulates the intersection of stress, social behavior, and metabolism. Fos expression in the MeA of mice is altered by fasting and hyper- and hypoglycemia, suggesting this nucleus may regulate feeding behavior and blood glucose levels in response to internal cues. Chemogenetic activation of MeA neurons produces two seemingly contradictory phenotypes: elevated blood glucose and suppressed feeding, independent of anxiety-like behavior. MeA neuronal projection targets include the principle nucleus of the bed nucleus of the stria terminalis (prBNST) and ventromedial hypothalamus (VMH), regions previously shown to regulate metabolism. Selectively activating MeA --> VMH projection neurons induces hyperglycemia and hypoinsulinemia. These results suggest that MeA --> VMH neurons may be activated during hypoglycemia to coordinate the return of blood glucose to normal levels. As activation of the MeA suppresses feeding, we hypothesize that this function is not homeostatic and may be regulated through other MeA projection targets (e.g., prBNST). Ongoing fos, axonal tracing, and behavioral studies aim to delineate the contributions of different MeA cell types to feeding and glucose homeostasis in the context of other competing behaviors including social interaction and stress.

5:45 **Central Inputs To Preproglucagon (Ppg) Neurons Revealed With A Cre-Conditional Pseudorabies Virus (Prv)**

MARIE K HOLT[1], LISA E POMERANZ[2], LINDA RINAMAN[1]

[1]Florida State University, Tallahassee, FL, United States, [2]Rockefeller University, New York City, NY, United States

The anorexic neuropeptide glucagon-like peptide-1 (GLP-1) is expressed in PPG neurons in the nucleus of the solitary tract (NTS). Central inputs to the NTS have been described, but little is known regarding circuits impinging on PPG neurons. Here, we identify circuits upstream of PPG neurons in transgenic PPG-Cre mice using a neurotropic virus, PRV-Introvert, which replicates and expresses GFP in a Cre-dependent manner. After infection of PPG neurons, GFP expression and retrograde viral transport are enabled to reveal polysynaptic inputs. Additional experiments investigated monosynaptic inputs to PPG neurons using EnvA-RABV-ΔG-GFP, and also determined non-cell-type-specific inputs to the mouse NTS using Cholera toxin subunit B (CTB). All injections were targeted to the NTS. Following PRV-Introvert injection, the number of GFP+ neurons in the NTS increased at 48, 72 and 96h post-inoculation in PPG-Cre but not wildtype mice. After 72h, GFP+ cells were present in additional areas also positive for CTB, including Barrington's nucleus (Bar), the hypothalamic paraventricular nucleus (PVN), lateral hypothalamus (LH), and parasubthalamic nucleus (PSTh). CTB+ NTS-projecting cells in these regions were activated by 30mins restraint stress (p's< 0.05), and monosynaptic inputs from PVN and PSTh to PPG neurons were documented. Within Bar and PVN, a subset of CTB+ NTS-projecting cells expressed mRNA for corticotrophin releasing hormone (CRH), a neuropeptide important in stress regulation. These novel anatomical tracing data reveal a structural basis for widespread CNS regulation of hindbrain PPG/GLP-1 neurons that inhibit food intake and shape other motivated behaviors, especially during times of stress.

6:00 - 8:00 PM	Transit Zone
POSTER SESSION I	

P1 **Classification And Selective Stimulation Of Colonic Enteroendocrine Cells Based On Single Cell Mrna Expression Analysis**

FRANK REIMANN[1], LAWRENCE BILLING[1], PIERRE LARRAUFIE[1], DEBORAH GOLDSPINK[1], RICHARD G KAY[1], GILES YEO[1], BRIAN LAM[1], LEITER ANDREW[2], FIONA M GRIBBLE[1]

[1]University of Cambridge, Cambridge, United Kingdom, [2]University of Massachusetts , Worcester, MA, United States

We aim to stimulate selective hormone release from enteroendocrine cells (EEC) to treat diabetes and obesity. Previously we have shown that colonic EECs co-express glucagon-like peptide-1 (GLP-1), peptideYY (PYY) and insulin-like peptide-5 (Insl5), which are co-released from a mostly overlapping vesicular pool (Billing et al. 2018). To address if different colonic enteroendocrine hormones could nonetheless be recruited differentially, we aimed to further subclassify different EECs using NeuroD1-CrexRosa26EYFP mice to FACsort colonic EECs for single cell mRNA sequencing. Based on their expression profile cells could be clustered into groups representing somatostatin expressing D-cells (n=167), GLP-1 expressing L-cells (3 clusters) and tryptophan hydroxylase 1 expressing EC-cells (4 clusters). EC clusters differed by Secretin (n=180), Tachykinin1 (n=131) or Piezo2 (n=236 and 238) expression. Two L-cell clusters expressed high levels of Insl5 (n=164 and 221), whereas the remaining cluster was distinguished by co-expression of neurotensin (Nts, n=280). Consistent with an observed relative selective expression of Agtr1a in the Insl5 L-cell and D-cell cluster, angiotensin II (10 nM) stimulated Insl5 and peptideYY release in primary epithelial cultures, but failed to stimulate Nts release, while stimulation of the more broadly expressed FFA1 with AM-1638 (3 mM) stimulated the release of all colonic L-cell products. Immunohistochemical and LC-MS based analysis of the colon further indicated that Nts expression is restricted to the proximal 3 cm of the mouse colon, whereas Insl5 expression increased towards the distal colon. This demonstrates that selective recruitment of colonic hormones is feasible and other selectively expressed receptors are to be investigated in the future.

P2 **Norepinephrine Stimulation Of Alpha 2 Adrenergic Receptors Inhibits Vagal Activation Of Catecholamine Neurons In The Nucleus Of The Solitary Tract In A Glucose Dependent Manner.**

M ZHU, S.M. APPLEYARD

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Catecholamine (CA) neurons in the nucleus of the solitary tract (NTS) are directly activated by solitary tract (ST) afferents, which include vagal afferents from the GI tract. NTS-CA neurons have also been shown to be activated by GI signals *in vivo* and activation of these neurons causes inhibition of food intake. Norepinephrine (NE) is released locally within the NTS. However, the effect of NE on NTS-CA neurons is not well understood. Here we use transgenic mice that express EGFP under the control of the tyrosine hydroxylase (TH) promoter to identify NTS-CA neurons. We then record from NTS neurons using patch clamp techniques in a horizontal brain slice that allows selective stimulation of ST afferents. We show that NE inhibits the amplitude of ST evoked excitatory post-synaptic currents (ST-EPSCs) in NTS-CA neurons in a concentration-dependent manner. The effects of NE are mimicked by dexmedetomidine, an alpha2 adrenergic receptor agonist, but not by phenylephrine or isoproterenol, alpha1 or beta adrenergic receptor agonists respectively. In contrast, the effect of NE is blocked by phentolamine, a non-selective alpha adrenergic receptor antagonist, as well as SKF86466, a selective alpha2 adrenergic receptor antagonist; but not by either prazosin or propranolol (alpha1 and beta adrenergic receptor antagonists). Interestingly, NE significantly inhibited the ST-EPSC amplitude in higher (5 and 10mM) glucose concentrations, but had no effect in lower glucose (2mM). These studies suggest a potential mechanism by which NE can inhibit vagal activation of NTS-CA neurons, which could in turn reduce NTS-CA neuron mediated inhibition of food intake. This could also be one mechanism by which NTS-CA neurons negatively feedback to reduce their own activation.

P3 **Involvement Of Vagal Afferents In Nutrient-Specific Satiation And Learned Taste Avoidance**

ELIZABETH LOXTERKAMP[1], LINDSEY A. SCHIER[2]

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The vagus nerve has long been thought critical for relaying meal-related information from the gut to the brain, but studying how these sensory signals are received and encoded has been hampered by the nerve's organization. The recent development of a method to make selective lesions of vagal afferent neurons (VANs) innervating the gut with injections of CCK-Saporin (250 ng/ul; 1.0 ul/side; CCK-Sap) into the nodose ganglia, while leaving other sensory and motor vagal fibers intact, now facilitates these investigations. Here, in order to test the hypothesis that VANs are critical for nutrient-driven satiation signals, male Sprague Dawley rats received bilateral CCK-Sap VAN lesions or sham surgery (blank-SAP) and were then given a series of 30-minute intake tests with different nutrient solutions while food deprived. CCK-Sap rats that failed to suppress sucrose intake ($\leq$ 25% reduction from baseline) in response to an IP CCK (10 ug/kg) treatment were included in the analyses (n = 6). Relative to Sham rats (n = 4), CCK-Sap rats tended to ingest more of a 4.5% corn oil emulsion but consumed comparable amounts of sugar solutions (0.56 and 1.1 M). To determine if VANs play a role in the rapid detection of emetic salt, LiCl, CCK-Sap and Sham rats were given 0.12 M LiCl to consume (20-min), while water

deprived, and both groups rapidly suppressed licking. However, after exposure to LiCl, CCK-Sap rats consumed significantly more of an isomolar, similar tasting, but innocuous, NaCl solution, suggesting an impairment in learned taste avoidance. CCK-Sap and Sham rats did not differ in body mass or 24-hour chow and water intake. Future studies will be key for elucidating the role of VANs in conveying temporally- and chemically-distinct signals critical for ingestive control.

P4 **Impact Of Early Life Gut Microbial Environment On Vagal Development And Cck-Induced Satiety**

ANNA K. KAMITAKAHARA[1], VALERIE M. MAGALONG[1], PAT LEVITT[1,2]

[1]Children's Hospital Los Angeles, Los Angeles, CA, United States, [2]University of Southern California, Los Angeles, CA, United States

Over 40% of pregnant women receive intrapartum antibiotics as prophylaxis against streptococcal infection, or during cesarean section. While antibiotic treatment reduces infection, it also alters the gut microbiota of newborn infants and is associated with an increased risk for development of childhood obesity and diabetes. The vagus nerve directly connects the brain and gastrointestinal tract, and is able to sense and fire action potentials in response to microbial signals. However, a critical knowledge gap exists in understanding whether microbiome disruption affects vagal development and metabolic function in neonatal life. To this end, we used a mouse model of perinatal antibiotic exposure: [1)] control mice receiving no antibiotics, [2)] mice receiving penicillin 1 week prior to birth through the end study (ABX^{Life}), and [3)] mice receiving penicillin 1 week before birth through 4 weeks of age, after which they were maintained on water with no antibiotics (ABX^{Early}). Preliminary data suggest that ABX^{Life} mice (23.1g, 0.907g [mean, SEM]) tend to weigh less than control mice (26.8g, 0.609g), while ABX^{Early} mice (27.8g, 0.538g) tend to weigh more at 12 weeks. In addition, body composition analysis revealed that both ABX^{Life} and ABX^{Early} mice exhibit a trend toward increased fat mass and decreased lean mass, compared to controls. To assess vagal signaling in early life, control and antibiotic treated pups were injected with choleocystokinin (CCK) on postnatal day 7. Pups receiving antibiotics tended to have a blunted CCK-induced cfos response in the nucleus of the solitary tract. While greater sample sizes are required to demonstrate statistical significance, these early trends suggest that early life antibiotic exposure may impair vagal afferent signaling of satiety.

P5 **Effects Of Intragastric Administration Of L-Tryptophan On Energy Intake And Postprandial Fullness And Hunger In Lean Men And Men With Obesity**

MARYAM HAJISHAFIEE[1], SINA S ULLRICH[2], ROBERT E STEINERT[3], MICHAEL HOROWITZ[1], CHRISTINE FEINLE-BISSET[1]

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Intraduodenal infusion of L-tryptophan (TRP), at a dose of ~3 g, increases fullness and markedly reduces energy intake, in healthy men. The effects of intragastric TRP (resembling oral intake, while avoiding the unpleasant taste of TRP) on fullness, hunger and energy intake, and whether responses differ in health and obesity, are uncertain. We investigated in 12 lean men (age 31±3 y; BMI 23±1 kg/m^2) and 13 men with obesity (age 31±3 y; BMI 33±1 kg/m^2) on three separate occasions, in double-blind, randomised order, the effects of 3 g (TRP-3) or 1.5 g (TRP-1.5) TRP, or control (C), on energy intake from a buffet meal offered 30 min later. Fullness and hunger were measured at baseline and in response to TRP alone, and for 2.5 h after the meal. TRP alone did not affect fullness or hunger in either group. TRP-3 markedly reduced energy intake compared with C in lean men (-216±64 kcal), and compared with TRP-1.5 (-205±86 kcal) and C (-237±62 kcal) in men with obesity (all $P< 0.05$). After the meal, despite markedly lower energy intakes after TRP-3, fullness was greater compared with C in lean men (AUC, min*mm; TRP-3: 5163±941, TRP-1.5: 4449±869, C: 4007±930, $P< 0.05$), and did not differ from C in men with obesity (AUC, min*mm; TRP-3: 5755±904, TRP-1.5: 6120±835, C: 5880±893), while hunger did not differ between treatments in either group. Thus, intragastric TRP has a potent energy intake-suppressant effect in both lean men and men with obesity, and is associated with sustained post-meal fullness, despite the substantially lower energy intake. Further studies are warranted to evaluate the effects of TRP on energy intake at subsequent meals (to investigate whether energy compensation occurs later), and the mechanisms underlying the observed effects.

P6 **Plasma Free Amino Acid Responses To Oral Whey Protein Consumption And Relationships With Gastric Emptying, Glucoregulatory Hormones And Energy Intake In Healthy, Lean Men**

AMY T HUTCHISON[1], RACHEL A ELOVARIS[1], KYLIE LANGE[1], MICHAEL HOROWITZ[1], CHRISTINE FEINLE-BISSET[1], NATALIE D LUSCOMBE-MARSH[1,2]

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Whey protein has potent effects to improve postprandial glycaemia and reduce energy intake, and both may be mediated by key amino acids (AAs). This study evaluated in 16 healthy men the effects of equally palatable 450-mL drinks containing increasing loads of whey protein isolate 30 g (L) or 70 g (H)), or saline (C), on plasma AA concentrations, and relationships with gastric emptying (GE), glucagon-like peptide-1 (GLP-1), insulin,

glucagon, blood glucose and energy intake, using a randomized, double-blind design. AAs and hormones were measured before and at regular intervals over 180 min, following each drink, and energy intake (kcal) from a buffet-style lunch was quantified afterwards. GE of the drinks (kcal/min) was evaluated for 180 min. GE of L and H was comparable (L:2.6±0.2, H:2.9±0.3). Both L and H increased concentrations of 19/20 AAs compared with C, but only 7/20 AAs were increased more by H than L. Incremental areas under the curve ($iAUC_{0\text{-}180min}$) of GLP-1 (R^2 range 0.62-0.68), insulin (R^2 0.60-0.65), and glucagon (R^2 0.60-0.85) were strongly and directly correlated with iAUCs of plasma AA concentrations, particularly leucine, isoleucine, lysine, tyrosine, methionine, tryptophan, glutamic acid and aspartic acid (all $P< 0.05$). Blood glucose was not correlated with AAs. Energy intake was correlated inversely and only weakly with 15/20 AAs (R^2 0.12-0.21, $P< 0.05$). Therefore, in healthy people following oral protein drinks, glucoregulatory hormones are strongly correlated with specific essential AAs, while there was no correlation with blood glucose, and the relationship with energy intake was weak. Thus, the factors mediating effects on blood glucose and energy intake are likely to be multifactorial, and their inter-relationships remain to be fully elucidated.

P7 **Intraoral Sucrose Intake And Consummatory Oromotor Responses Following Roux-En-Y Gastric Bypass In Rats.**

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After Roux-en-Y gastric bypass (RYGB), rats decrease intake of and preference for high concentrations of sucrose. Some have suggested that this is due to decreased palatability of the sugar solution, but this view is not universally held. To further interrogate this issue, we implanted an intraoral cannula in rats that previously underwent RYGB (6/sex) or SHAM (6 M; 9 F) surgery. These rats were tested for intraoral intake of water (1 day) and then of 1M sucrose (8 days). Infusions (1ml/min) lasted until the rat rejected the solution. Volume consumed was measured. Video-recorded oromotor responses to water and to the first and last sucrose sessions were later scored (blind) for the: a) first 30s, b) 30s prior to stimulus rejection, and c) 30s after the infusion ended. RYGB rats consumed less sucrose than SHAM rats (Ps< 0.01). All groups showed similar high levels of ingestive oromotor responses at the start of sucrose sessions, which decreased somewhat leading up to the first stimulus rejection. Interestingly, by the last day of sucrose testing, RYGB rats displayed a larger number of aversive responses at the end of the session, compared to: a) SHAM rats, b) water, c) day 1 sucrose (Ps< 0.01). These signals do not appear to condition a taste aversion, though, as early oromotor behaviors do not change (Ps>0.14). Thus, lower intake in RYGB rats does not seem to reflect a decrease in the unconditioned or conditioned affective taste properties of sucrose. However, the eventual emergence of aversive oromotor responses specifically in RYGB animals at the end of the session suggests that a negative visceral state beyond normal satiation leads to termination of swallowing, and with experience manifests in oromotor behavior reminiscent of the concepts of nimiety or alliesthesia.

P8 **Differential Effects Of A High Fat/Sucrose Diet Versus A Low Fat Diet On Glucose Homeostasis And Beta-Cell Sensitivity In A Rat Model Of Gastric Bypass Surgery**

WARNER HOORNENBORG[1], EDIT SOMOGYI[1], JAN BRUGGINK[1], THOMAS LUTZ[2,3], CHRISTINA BOYLE[2], MARLOES EMOUS[4], ANDRE VAN BEEK[5], GERTJAN VAN DIJK[1]

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Roux-en Y gastric bypass (RYGB) surgery is the only sustainable treatment of morbid obesity, not only for its weight reducing and hypophagic effects, but also for the marked improvements of metabolic co-morbidities. In fact, obese patients undergoing bariatric surgery frequently have remission of type-2 diabetes mellitus. It is not clear whether and how the habitual diet affects behavioral and metabolic outcomes following RYGB. For this reason, we investigated ingestive behavioral and glucose homeostasis parameters in 5 month-old male Wistar rats that were maintained chronically either on a low-fat chow diet (LF, n=6-8) or a high fat/sucrose chow diet (HFS, 6-11) in pelleted form, before and after RYGB. While RYGB caused considerable weight loss over 4 weeks, this weight loss was most outspoken in the HFS group (-30% versus -20% in the LF group), with reduction in fat mass but not lean mass contributing to this phenomenon. Energy intake was most profoundly reduced by RYGB in the HFS group (-50%) relative to the LF group (-25%). Meal size, but not meal frequency or intermeal interval changed significantly by RYGB, with a significantly higher satiety ratio increase in the HFS feeding rats than found in the LF group. Glucose homeostasis assessed at baseline (HOMA-IR) and assessed by a mixed meal tolerance test (MMT) showed improvements of insulin resistance and beta cell sensitivity irrespective of diet, however, rats on the HFS (but not on the LF diet) became glucose intolerant after RYGB surgery in the MMT test. Our results show that post-RYGB glucose homeostasis in HFS feeding rats appeared deranged despite most profound reductions in weight loss and increased satiety.

P9 **Effects Of Roux-En-Y Gastric Bypass On Sugar-Associated Flavor Preference Learning In Rats**

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In rodents, repeated exposures to isocaloric glucose and fructose, two sugars with different metabolic pathways, eventually induce a higher preference for glucose or a glucose-associated flavor. Because after Roux-en-Y gastric bypass (RYGB), rats decrease their intake of and preference for sugar solutions in long-term tests, here we tested whether RYGB rats would demonstrate a glucose-conditioned flavor preference. Rats with RYGB (male, n=11; female, n=10) or sham (male, n=9; female, n=10) surgery were exposed for 30 min to 2 bottles containing 8% glucose or fructose differentially flavored with either 0.05% grape or Kool-Aid (4 days), with sugar/flavor pairings counterbalanced, then to one bottle with flavored glucose or fructose (8 days, alternating). This training was followed by 2-bottle tests of the glucose-paired (CS+) vs. the fructose-paired (CS-) flavor as follows: 8% glucose/CS+ vs. fructose/CS- (Test 1), CS+ vs. CS- both mixed in 4% glucose + 4% fructose (Test 2); CS+ vs. CS- both in 0.2% saccharin (Test 3); CS+ vs. CS- in water (Test 4). All groups preferred the glucose/CS+ on Test 1, demonstrating that RYGB did not disrupt the acquisition of glucose preference (Ps< .01). When differential sugar cues were removed, but a sweetener was present (Tests 2 & 3), all groups preferred the CS+ flavor (Ps< .03), except for female RYGB rats. Decreased CS+ flavor preference was evident in all groups by Test 4 (all Ps< .01). These results suggest that the positive effects of experience with glucose ingestion leading to acquisition of flavor preferences are not dependent on the sugar contacting the stomach, duodenum, or proximal jejunum, but acquired preferences for glucose-paired flavors may be more vulnerable to generalization decrement or extinction after RYGB in female rats.

P11 **Early Life Consumption Of Low-Calorie Sweeteners Influences Ingestive Behavior During Adulthood**

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Over the last 20 years, consumption of low-calorie sweeteners (LCSs) increased by 200% among U.S. children. Given that LCSs pair sweet taste with little to no calories, it is imperative to understand how LCS consumption during critical periods of development influences ingestive behavior later in life. Here we examined whether early life (postnatal, PN days: 26-77) daily consumption of LCSs (acesulfame potassium [AceK], saccharin, or stevia) in male and female rats affects various components of ingestive behavior when tested during adulthood (PN 89-193). Importantly, LCS consumption was restricted to PN 26-77 (prior to behavioral testing) and limited to the FDA-established acceptable daily intake levels (based on mg/kg body weight). To examine whether early life LCS consumption influences taste- and/or postingestive-driven ingestive behaviors for sugar or non-sugar substances, we measured [1] licking behavior in short-term (30-min) tests (for 0.56 M glucose vs fructose, and 0.15-1 mM quinine), [2] willingness to work for sucrose pellets in an operant progressive ratio (PR) task, and [3] 4-week ad libitum consumption of 11% sucrose in the home cage. Independent of sex and sweetener, early life LCS consumption augmented taste-driven licking for 0.56 M fructose over equimolar glucose. However, LCS consumption had no effect on licking for a prototypical “bitterant” quinine. LCS-exposed rats also showed reduced motivation to work for sucrose in a PR test. However, when tested under free-feeding conditions in the home cage, LCS-exposed rats consumed more sucrose than controls. In summary, habitual consumption of LCSs during the juvenile and adolescent stages produces long-lasting effects on ingestive behavior that may promote excessive sugar consumption later in life.

P12 **Repeated Chemogenetic Activation Of Hindbrain Catecholamine Neurons In The A1/C1 Cell Group Decreases Subsequent Feeding Responses To Both Chemogenetic And Glucoprivic Activation**

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Protective responses to acute glucose deficit, known as counterregulatory responses (CRRs), are elicited robustly by acute glucoprivation, but repeated episodes of glucoprivation can impair these responses, leading to a potentially lethal condition known as hypoglycemia associated autonomic failure (HAAF). HAAF is a major threat to diabetic patients on insulin therapy. Previous results strongly support the hypothesis that catecholamine (CA) neurons in the C1 and possibly the rostral A1 cell group of the ventrolateral medulla (VLM) are necessary and sufficient for elicitation of key CRRs, including food intake. Here we tested the hypothesis that repeated CA neuron activation, even in the absence of glucoprivation, would result in development of HAAF. Accordingly, a Cre-dependent DREADD construct, AAV2-DIO-hSyn-hM3D(Gq)-mCherry was stereotaxically injected bilaterally into the VLM A1/C1 overlap region of Th-Cre+ transgenic rats. This procedure produced a highly selective and effective transfection of CA neurons at the injection site, as reported in our published work. Systemic injection of the DREADD agonist, clozapine-N-oxide (CNO; 1 mg/kg), evoked a feeding response equivalent in magnitude to that produced by systemic injection 2-deoxy-D-glucose (2DG; 200 mg/kg). However, daily injection of either CNO or 2DG for four consecutive days resulted in abolition of the feeding response to CNO when tested on day 5. Our results demonstrate for the first time that repeated selective activation of A1/C1 neurons mimics HAAF, even though repeated CNO administration does not produce glucoprivation. These observations suggest that desensitization of A1/C1 CA neurons by repeated activation may be a major contributor to development of HAAF.

P13 **Ls Glp-1R Expressing Neurons Project To Distinct Feeding-Relevant Areas**

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Glucagon-like peptide 1 receptors (GLP-1R) are expressed in the lateral septum (LS) of rats and mice. We have shown that GLP-1 signaling in the LS plays a physiological role in the control of food intake under both non-stressed and stressed conditions and affects motivation for food in both species. To identify potential mediatory pathways for these effects, we determined the efferent projection pattern of LS GLP-1R-expressing cells. To produce cell type-specific anterograde labeling, we injected the LS with an AAV encoding a cre-inducible green fluorescent protein (GFP) in mice that express cre recombinase under the control of the GLP-1R promotor. We assessed a series of sections throughout the brain and determined the optical density of GFP+ fiber fields. As expected, we found dense projections to hypothalamic nuclei, hippocampus, and the VTA. Other areas including the BNST, hippocampus, and amygdala contained GFP+ fibers. The projection from LS GLP-1R expressing cells to the LH was the strongest observed (1.69 ± 0.13 OD units relative to 0.76 ± 0.01 OD units in a background/blank location), suggesting that this pathway may play a particularly important role in feeding control. By contrast, we saw few/no GFP+ fibers in the PVN (0.86 ± 0.04 OD units). The projections we observed here were similar to those previously described in non-cell type specific tracing studies in rat, suggesting that GLP-1R cells in this region are representative of the general population of LS neurons, rather than a subgroup that project to a more select set of targets. This conclusion relies on the assumption that LS projections are the same in rat and mouse, and we are currently performing non-specific anterograde tracing in wildtype mice to make this comparison.

P14 **Selective Chemogenetic Activation Of Ventral Hindbrain Glia Cells Enhances Glucoprivic Feeding In Rats**

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Catecholamine (CA) neurons in A1/C1 region of the ventrolateral medulla (VLM) are required for key protective responses to glucose deficit (i.e., counterregulatory responses or CRRs), including glucoprivic feeding. Recent in vitro studies, however, indicate that glia cells also might play a role in glucoregulation. The possibility that glia and A1/C1 CA neurons in VLM might cooperate to mediate glucoregulatory responses has not been assessed. As an initial test of this hypothesis, we used an AAV5 vector to selectively transfect glial cells in the vicinity of the A1/C1 area to express hM3D(Gq)-mCherry driven by the glial fibrillary acidic protein (GFAP) promotor. Immunohistochemical analysis of mCherry, GFAP and dopamine beta-hydroxylase revealed highly selective and efficient transfection of glial cells, but not CA neurons at the injection site in the VLM. Transfected rats were tested for feeding in 4-hr tests in response to systemic injection a DREADD receptor agonist, clozapine-N-oxide (CNO; 1 mg/kg) or clozapine (0.1 mg/kg), following a subthreshold dose of the antiglycolytic agent, 2-deoxy-D-glucose (2DG; 50 mg/kg), or saline. None of these agents increased feeding when administered separately. However, when clozapine or CNO was injected 30 min after the 2DG injection, 2DG-induced food intake was significantly increased. Our results indicate that during glucoprivation, activation of VLM glial cells markedly increases the sensitivity or responsiveness to glucose deficit of neighboring A1/C1 CA neurons. These observations provide the first in vivo evidence for glial contribution to mediation of a glucoregulatory response in non-anesthetized animals.

P15 **5-Ht2C And 5-Ht3 Receptors Mediate The Neural Activation Of Nts Glp-1 Neurons By Aversive But Not Rewarding Stressors**

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Despite a growing appreciation of downstream nuclei targeted by the central GLP-1 system, the neurosubstrates that activate preproglucagon (PPG) neurons remain unclear. Recent findings show that central serotonergic axons synapse on PPG neurons. Data from our lab shows the presence of mRNA transcripts for both 5-HT2CR and 5-HT3R on PPG neurons with co-expression of both transcripts on 55% of PPG neurons. Next, we examined the relative contribution of 5-HT2CR and 5-HT3R signaling in mediating PPG neural activation following administration of two behaviorally different pharmacological compounds known to activate PPG neurons, LiCl and cocaine. Rats were pre-treated 4th icv with 5-HT2CR or 5-HT3R antagonists (RS102221 and ondansetron, respectively) followed by systemic administration of either LiCl or cocaine. Our results show that blockade of either 5-HT2CR or 5-HT3R is sufficient to block the increased c-Fos in PPG neurons induced by LiCl, but neither had an effect on c-Fos activation of PPG neurons following cocaine. These results suggest that PPG activation following a visceral stressor is achieved via a central 5-HT2C- and 5-HT3-dependent mechanism when the stressor drives a malaise like response; however, neural activation of the central GLP-1 system by cocaine does not involve 5-HT2C or 5-HT3-mediated signaling. Behavioral confirmation of this conclusion was revealed by showing that blockade of 5-HT3R, but not 5-HT2CR, reversed the acute anorectic effects of LiCl. Collectively, our findings indicate that LiCl activates PPG neurons via a central serotonergic mechanism,

predominately via hindbrain 5-HT3R activation. Current experiments are focused on identifying the central source of 5-HT responsible for the modulatory effects on PPG neurons. NIH-DK115762, DA037897.

P16 **Glucagon-Like Peptide-1 Receptor Activation In The Laterodorsal Tegmental Nucleus Regulates Cocaine-Mediated Behaviors Via A Gabaergic Mechanism**

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Central glucagon-like peptide-1 receptor (GLP-1R) activation has been shown to regulate motivated behaviors, including addiction-like phenotypes. The laterodorsal tegmental nucleus (LDT) is a region that plays a critical role in the reinstatement of cocaine-seeking behavior, an animal model of relapse. Previous studies in our lab have shown that LDT GLP-1R activation via exendin-4 (Ex-4) reduces cocaine reinstatement. However, the mechanisms by which Ex-4 acts in the LDT to decrease cocaine seeking remain unclear. Based on our pilot studies that systemically administered Ex-4 binds to putative GLP-1Rs expressed on LDT GABAergic neurons, we hypothesized that the efficacy of Ex-4 to reduce cocaine seeking is due, in part, to activation of LDT GABA neurons that project to the VTA. To investigate the functional role of LDT GABA GLP-1Rs in cocaine seeking, we selectively knocked down GLP-1Rs expressed on GABA neurons using a cre-dependent GLP-1R shRNA infused into the LDT of GAD-Cre rats. Decreased expression of GLP-1Rs exclusively on LDT GABA neurons partially prevented the ability of Ex-4 to reduce cocaine seeking. These findings indicate that endogenous GLP-1 signaling in LDT GABA neurons is functionally relevant for modulating cocaine-seeking behavior. We then hypothesized that Ex-4 reduces cocaine seeking by activating GLP-1Rs on LDT GABA neurons that project to the VTA. We selectively inhibited LDT GABAergic projections to the VTA using chemogenetic methods and subsequently tested the ability of systemic Ex-4 to reduce cocaine seeking. We found that inhibiting LDT GABA terminals in the VTA partially blocked the efficacy of Ex-4 to reduce cocaine seeking. These data suggest that Ex-4 regulates cocaine reinstatement by activating LDT GABAergic projections to the VTA.

P17 **Effects Of Diet On Brainstem Gliosis: Implications In The Pathophysiology Of Obesity**

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Human and rodent studies show that exposure to a high fat diet (HFD) induces activation of hypothalamic glial cells, hypothesized to result in a state of chronic, low-grade hypothalamic neuroinflammation. The dorsal vagal complex (DVC) is another critical CNS structure involved in the neural regulation of energy balance; however, there is a paucity of information regarding DVC glial contribution. We performed immunohistochemical (IHC) analyses to determine the effect of diet, energy state, obesity, and leptin on DVC gliosis. IHC quantification of GFAP intensity (astrocyte activation marker) and Iba1 positive cells (microglial marker) after 8 weeks HFD maintenance in male rats, showed a surprising decrease in DVC astrogliosis with an increase in Iba1+ cells compared to chow-fed controls. In diestrus females, HFD also induced a decrease in DVC astrogliosis, but had no effect on microglia density, indicative of a sex-dependent difference. To delineate between potential drivers (diet and/or obesity-associated hyperleptinemia), we utilized the Zucker diabetic fatty rat (ZDF) which are hyperphagic, obese and lack leptin receptor signaling. Compared to wild type, ZDF rats exhibited lower levels of DVC GFAP expression, suggesting the obesity-driven reduction in astrogliosis is leptin-independent. In support of this hypothesis, one week of daily leptin injections into the DVC did not affect astrogliosis. Interestingly, we observed a significant *increase* in DVC astrogliosis in rats pair-fed to match the leptin-induced body weight suppressive effects. These collective findings are in stark contrast to the HFD-induced hypothalamic gliosis observed in previous studies and warrants further investigation into nuclei specific effects of energy state on non-neuronal cells.

P18 **Mixed Feelings And Emotion Regulation In Obesity**

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Emotion regulation has been studied in the context of obesity and was found to influence food intake. Besides, food stimuli can elicit mixed feelings (i.e. simultaneous feelings of both pleasant and unpleasant emotions) when they trigger conflict between pleasure and health-related goals. However, our understanding of the affective processes involved in overeating and obesity remains incomplete. We thus first investigated emotion regulation and mixed feelings in underweight (n=21), healthy weight (n=27), overweight (n=22) and obese individuals (n=11). Compared to the healthy controls, we expected obese participants to report more mixed feelings and to have lower emotion regulation performances. We also wanted to explore the underweight and overweight groups. Participants rated positive, negative and mixed film clips on amusement and repulsion. Half of them were instructed to watch the film clips, while the others were asked to reinterpret the content of the film clips. As expected, obese individuals reported more mixed feelings than the underweight (p=.01), healthy weight (p=.01)

and overweight (p=.004) individuals in the watch condition. They did so not only for the mixed (p=.01, p=.04, p=.002 respectively), but also for the negative film clips (p=.005, p< .001, p=.001 respectively). Surprisingly, they showed better emotion regulation performances than the underweight (p=.02), healthy weight (p=.01) and overweight (p=.04) participants. Besides, our results did not reveal any significant difference for the underweight nor for the overweight group, compared to the healthy controls. These results encourage a replication with a larger sample of participants. We are currently conducting this replication with healthy weight and obese individuals.

P19 **Higher Bmi Is Associated With Lower Lateral Prefrontal Cortex Activation During Food Choices When Healthiness Is Considered**

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People make many food choices per day. Unhealthy food choices can contribute to weight gain. This study examined whether people with a higher BMI make more unhealthy food choices and what the influence of BMI is on the neural activation during their food choices. 153 participants (86F, age 44.4±4.8y, BMI 18-47 kg/m^2) were scanned with fMRI while performing a food choice task. During this task participants were asked to consider the healthiness or tastiness of the food or choose naturally. Afterwards they provided health and taste ratings. Behavioral analyses showed that participants with a higher BMI made healthier food choices when choosing naturally. Although overall participants chose healthier foods when considering healthiness, there was a negative correlation with BMI. Imaging results show a negative correlation between BMI and activation in the right lateral prefrontal cortex when considering healthiness (cluster-level P_{fwe}< 0.05, Z=4.40). In conclusion, when choosing naturally individuals with a higher BMI do not make more unhealthy choices and BMI does not affect their neural activation. However, when asked to consider the healthiness of the foods during choice individuals with a higher BMI do not adapt their choice behavior towards healthier choices and accordingly show lower activation in a brain area involved in cognitive control. This suggests that individuals with a higher BMI may have more difficulty improving the healthiness of their food choices.

P20 **Impairment Of Negative Outcome Learning In Obesity May Depend On The Type Of Reward**

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Obesity is associated with impaired negative but not positive outcome learning. Previous studies have notably shown this impairment with monetary gain/loss and positive/negative feedback (i.e., “correct”/“incorrect”) in probabilistic learning tasks. In the current study we examined probabilistic learning with food reward in 30 healthy weight (HW) and 27 obese (OB) participants. During the acquisition phase, participants learned to choose between three different pairs of stimuli (AB, CD, EF) based on probabilistic feedback. A was the most rewarded stimulus (positive feedback in 80% of trials) and B the least rewarded one (positive feedback in 20% of the trials). A feedback was provided after each trial. Correct responses were rewarded with “you won an M&M’s®!” while a picture of a plate full of M&M’s® was presented on the screen. Participants could eat the M&M’s® they won at the end of the experiment.After incorrect responses, “you did not win an M&M’s®” and a picture of an empty plate were presented on the screen.During the testing phase, novel pairs were presented (AC, AD, AE, AF, BC, BD, BE, BF) and no feedback was provided. Both healthy-weight (HW) and obese (OB) individuals had a higher accuracy score with novel pairs involving to choose A (HW: 71,67% ± 23,68; OB: 72,33%± 18,52) than to avoid B (HW: 60,42% ± 24,94; OB: 64,12% ± 22,56). In other words, both groups were better at choosing the most rewarded stimulus than avoiding the less rewarded one. There was neither a significant effect of the group nor an interaction between the type of trials and the group. These findings suggest that deficits in negative outcome learning in obesity may depend on the type of reward used in experimental tasks.

P21 **Grab To Eat! Eating Motivation Dynamics Measured By Effort Exertion Depend On Hunger State**

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A crucial challenge in investigating motivated human eating behaviour is to go beyond subjective and static measures, by developing reliable methods capable of objectively quantifying the dynamic aspects of appetitive motivation. Therefore, we developed and tested a novel effort-based task (Grab-to-Eat Task (GET)) which utilises handgrip force as a motivational measure to capture eating motivation dynamics throughout consumption. Sixty normal-weight young adults (*23.4±3.0 y; 22.1±1.9 kg/m^2*) were randomly allocated to one of two hunger state conditions (hungry or satiated). They performed a continuous reinforcement-based task, during which 12-g sips of chocolate milk were self-administered with a handgrip force transducer. Motivation was covertly assessed by the magnitude of effort exertion towards each sip. Cumulatively, hungry subjects exerted

more effort (M_h = *497±334kPa;* M_s= *343±249kPa; p = 0.009*) and consequently consumed more chocolate milk than satiated ones (M_h =*13.2±6.8 % of TDEE;* M_s= *9.6±5.4 % of TDEE; p = 0.035*). Effort exertion declined throughout consumption in both hunger state groups (*p < 0.001*), with the rate of decline being two-fold greater in hungry subjects *(p = 0.013)*. Furthermore, effort exerted in the initial stages of consumption predicted subsequent intake (r_h= .402, r_s = .389). Present results fit in the theoretical framework of reward-related motivation and suggest that the developed paradigm is sensitive to eating motivation dynamics throughout consumption and to changes in eating motivation induced by hunger state manipulation. Further validation, ideally involving functional neuroimaging, would be imperative. In the future, the paradigm couldbe used to investigate eating motivation dynamics in various populations, conditions and food products.

P22 **Irrational Beliefs, Emotional Eating, And Food Misuse**

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Irrational beliefs (IB) or cognitive distortions, hypothesized in cognitive behavioral therapies to be a prime cause of psychological maladjustment, are associated with a wide variety of psychopathologies including disordered eating (including poor interoceptive awareness, bulimia symptoms, and body dissatisfaction), poor self-esteem, avoidant coping strategies, depression, anxiety, and addictive behaviors (e.g., gambling and alcohol). IB may be related to dietary restraint but its role in emotional eating (EE) has not been examined. Furthermore, research in "food addiction" (FA) has increased but has not been examined in regard to IB. Like IB, FA is associated with anxiety, depression, and disordered eating. The relationship between IB (Shortened General Attitude and Belief Scale) and eating styles (DEBQ), anxiety, depression, FA, and BMI were examined in 192 (72.4% women) adults. The results confirmed positive associations between IB and depression and trait anxiety. IB were positively associated with EE (r=.335, p=.000) and positively correlated with FA symptoms (r=.273, p=.000). There was no correlation between IB and BMI (r=-.018, p=814). As predicted, the relationship between IB and FA was mediated by EE (but not anxiety). Exploratory mediation analysis indicated that there was a significant indirect (but not direct) pathway between IB and higher FA; IB elevated anxiety which elevated EE which elevated FA (B = .02, SE = .01, 95%CI = .004 - .033). The total effects model was significant (adjusted R^2=.07). The mediation of the association between IB and FA by EE was due to anxiety and not depression. Consideration of irrationality in cognitions may be productive, especially when examining maladaptive eating behaviors.

P23 **Attachment Anxiety, Affect Regulation And Night Eating**

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Night eating syndrome (NES) is associated with stress and maladaptive eating behaviors such as emotional eating (EE) and “food addiction” suggesting that emotion regulation is a key component in the expression of NES. Thus, the goal of the current study was to investigate NES considering attachment theory which contains a conceptual framework that has been widely used to understand emotion regulation and its management with external substances such as food. We examined whether attachment insecurity was associated with NES. In addition, we examined whether EE and/or uncontrolled eating (UE) mediated any relationship between the two (pre-registered hypotheses). 275 British and American adults participated via an online platform. Questionnaires measured EE and UE, attachment anxiety and avoidance, and NES. Body mass index was calculated from reported height and weight. There was a significant direct relationship between attachment anxiety and NES that remained evident when mediators were included in the model (*B* = 1.74, *SE* = .24, *LLCI* = 1.26 & *ULCI* = 2.25, *p* < .001) but no significant indirect relationships via either UE (*B* = .02, *SE* = .04, *LLCI* = -.04 & *ULCI* = .11) or EE (*B* = -.01, *SE* = .03, *LLCI* = -.08 & *ULCI* = .05) were found. The overall R^2 was .21. This failure to detect mediation may have been due to methodological issues such as questionnaire selection or lack of power. Alternatively, it may reflect an explanation based on reverse causality, i.e., NES may be associated with specific interpersonal issues that are reflected in attachment orientations. A follow-up study will explore these possibilities via the inclusion of additional measures and the use of a larger sample size.

P24 **Appearance-Related Media Affects Implicit Cognitive Responses To Food**

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This study investigated how exposure to commercials containing thin or plus-size models affects women’s implicit cognitive responses to food. One hundred sixteen college-age women watched a neutral documentary that contained a commercial depicting either a thin woman (n = 39), a plus-size woman (n = 38), or a commercial with no human actors (n = 39). After the documentary, women completed the flanker task to measure their implicit attention to foods. Results revealed those who viewed the commercial of the plus-size model experienced more response conflict in the flanker task on trials in which the healthy food targets were flanked by unhealthy distractor foods, whereas those who viewed the thin model or the neutral commercial did not. These results suggest that after viewing a commercial of a plus-size model, women are more easily distracted by unhealthy foods and as a result, may be more motivated to consume unhealthy foods.

P25 **The Food Macronutrient Composition Impacts Human Risk Decision**

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Neurotransmitter serotonin plays a key role in human behavior and mood, being the major target for the depression and anxiety disorder treatment. Previous studies show the pharmacological challenge in serotoninergic system modulates human risk decisions in a body-weight dependent manner. Here, we test whether a macronutrient manipulation of a meal can change human serotonergic system similar to the pharmacological challenge by assessing the changes in plasma tryptophan, neural responses and risk decision making. 32 male subjects were investigated in two different days with a gap of 7-9 days. They ate either a low- or a high-carb breakfast and the following temporal dynamics of plasma tryptophan was observed. Participants performed a risk decision-making task while their neural responses were assessed by means of functional magnetic resonance imaging. After a high vs. low-carb breakfast, we observed a significant increase in plasma tryptophan level that interacts with individual bodyfat in modulating risk decisions. On the neural level, the high- compared to low-carb meal increased activation in a set of the front-parietal regions, that has been previously shown to be relevant for risk-processing. We further identify subregions within this brain network, of which activities 1) are sensitive to the meal-induced tryptophan fluctuation, 2) are modulated by the individual differences in body fat and 3) further predict the meal-induced risk-shift in decision making. Our results demonstrate that the macronutrient composition of a meal can induce changes that mimic the pharmacological modulation of serotonergic system on neural and behavioral level depending on individual body composition.

P26 **Children'S Attentional Bias Toward Fruits And Vegetables As A Function Of Exposure And Food Neophobia**

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Previous research that has investigated attentional bias to food stimuli using a visual dot-probe task has found that children who are food neophobic show attentional biases toward unfamiliar relative to familiar food stimuli. This finding has been interpreted to mean that neophobic children perceive novel foods as threatening. In an attempt to replicate and extend this finding, the present study measured attentional bias in 78 children between the ages of 7-10 years, to pictures of a range of familiar and unfamiliar fruits and vegetables relative to visually matched neutral stimuli. Results revealed that on average, children showed an attentional bias away from the fruits and vegetables regardless of their levels of neophobia. However, among children who have low levels of neophobia, those who had tried a greater proportion of the food stimuli showed stronger attentional bias toward the foods. No such relationship was observed for neophobic children. These results suggest that children's attentional bias toward foods may reflect willingness to try the foods, whereas attentional bias away from foods may reflect avoidance. Although these findings do not infer causation, they suggest that for those children who are less neophobic, exposure to a variety of healthy fruits and vegetables may reinforce their willingness to eat these foods.

P27 **Development And Pilot Testing Of A Set Of Food Images For Use In The Study Of Eating Behaviors In Children**

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Food images are used to investigate the cognitive and neurobiological mechanisms of eating behaviors, but the lack of standardized image sets limits cross-study comparisons. We developed a set of matched (e.g., contrast, color saturation) images that included 30 high-energy-dense (ED) foods, 30 low-ED foods, and 30 office supplies photographed in 2 amounts (i.e. large or small quantity of peas or pens). Recognition was assessed by asking children to name the food or object. Children also rated emotional valence (1=very sad, 5=very happy) and excitability (1=very bored, 5=very excited). After initial testing, 1 high-ED, 2 low-ED, and 2 office supplies (10 images) were replaced due to low recognition; thus, differences between image Set 1 and Set 2 were analyzed. Children (6-10 years) from Central Pennsylvania rated Set 1 (n=30 children) and Set 2 (n=20 children). Differences in mean scores were evaluated with mixed linear models with least square means differences. Changes made between Set 1 and Set 2 improved recognition of lower-ED foods (Set 1=88.6±0.01% vs. Set 2=96.1±0.02%; P=0.002) and office supplies (84.0±0.2% vs. 91.6±0.03%; P=0.033). Excitability and emotional valence scores did not differ by amount or Set (all P's>0.08). However, scores were significantly different for high-ED, low-ED, and office supplies (P's < 0.0072), and high-ED foods were rated highest in excitability (4.1±0.1) and emotional valence (4.0±0.1) scores, followed by low-ED foods (3.1±0.1 and 3.5±0.1) and office supplies (2.9±0.1 and 3.2±0.1).

Using foods and items familiar to children, this high-quality image set elicited hypothesized differences in excitability and emotional valence between high- and low-ED foods, but responses to small and large amounts (i.e., portion sizes) did not differ.

P28 **Perceived Stress And Diet Quality In Pregnant Women With Overweight/Obesity: A Detailed Examination Of The Healthy Eating Index And Its Components**

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High perceived stress in the general population has been linked to greater total calorie intake and larger intake of calories from fat and sugar. Little is known, however, about the association between stress and diet quality during pregnancy, a time when minimizing stress and eating healthily are beneficial to mothers and the developing fetus. We hypothesized that higher levels of perceived stress would be negatively associated with diet quality. Pregnant women with overweight/obesity (*N*=249; *M* age=28.52 years [*SD*=5.52]; *M* BMI=34.11 kg/m^2 [*SD*=6.98]) completed prenatal demographic and perceived stress measures, and a 24-hr food recall (Nutrition Data System for Research). Height and weight were measured. Participants completed a telephone food recall with research staff within one week of the assessment. Food recall data were used to calculate the 13 Healthy Eating Index (HEI) components (e.g., total vegetables, whole grains, saturated fats) and the HEI total score (0-100 scale; higher scores reflect adherence to dietary recommendations). A Benjamini-Hochberg (B-H) adjustment was applied. Mixed effects models (adjusted for food recall day) indicated that greater stress was significantly associated with lower total vegetable, total fruit, whole fruit, and whole grain intake, and HEI total scores (*p*s=.0006-.01). However, after adjustment for relevant demographic variables (age, race, education, income, BMI), stress related only to lower total fruit intake (*p*=.02), a relationship that became nonsignificant after the B-H adjustment. Findings suggest that stress may be related to poor prenatal diet quality and lower intake of nutritionally healthy foods, although important demographic characteristics are more strongly associated with diet quality.

P29 **Perinatal Exposure To A Maternal Diet Varying In Protein Quantity And Quality Affects Body Weight And Adiposity Of Female Adult Offspring In Rat**

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Perinatal exposure to a specific maternal diet can affect offspring's health in adulthood. This work aimed to evaluate the consequences of different quantities and qualities of protein in the maternal diet during gestation and lactation on overweight risk in female offspring subjected to dietary self-selection (DSS). Dams (6 groups) were fed with a high-protein (HP; 47% protein) or a normal protein (NP; 19% protein) isocaloric diet during gestation containing either cow's milk (M)-, pea (P)-, or turkey (T)-derived protein. During lactation, dams were all fed with an NP diet (protein source unchanged from gestation). From postnatal day (PND) 28 to 70, pups (n=8/group) were subjected to DSS feeding with five cups containing HP-M, HP-P, HP-T, carbohydrates or lipids. Food intake and weight gain were recorded daily. Body composition, fasting plasma insulin and leptin levels were assessed on PND70. During lactation and the postweaning period, pups from the T and P groups had a lower weight gain compared to M group ($p< 0.0001$). During DSS feeding, food intake was not different between groups. On PND70, adiposity was affected in response (i) to maternal protein source, with a lower total adipose tissue (% of body weight) in the P and T groups compared to M group ($p< 0.0001$), and (ii) to maternal protein quantity, with an increased (≥ 16%) total adipose tissue in the HP than in NP gestation groups ($p=0.03$) associated with an increased leptin level ($p< 0.05$). No variation was observed for insulin level in plasma. Maternal protein source consumed during gestation and lactation affected body weight and body composition of the offspring. Regardless of the maternal source, an HP diet during gestation resulted in a higher adiposity and increased risk of overweight in the offspring.

P30 **Decision Making In A Child-Appropriate Version Of The Iowa Gambling Task Differs By Child Weight Status And Maternal Bmi**

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Children with obesity exhibit impaired decision making which may contribute to excess food consumption, but the extent to which familial obesity risk (maternal BMI) moderates this relationship is unclear. Thus, we examined the effect of maternal BMI on performance across blocks during a child-adapted version of the Iowa Gambling Task (Hungry Donkey Task; HDT) in children with healthy weight (HW) and overweight/obesity

(OB). Children (7-11 years; N=35 with HW; N=35 with OB) completed the HDT. Outcomes were (1) net score: number of "advantageous" minus "disadvantageous" choices, (2) win-stay (WS): proportion of trials where the same choice was selected after a gain, and (3) lose-shift (LS): proportion of trials where a different choice was selected after a loss. Linear mixed-effects models tested the effects of block (5 with 40 trials each), child weight status (HW, OB), and maternal BMI on outcomes. There was a block by child weight status interaction for WS ($p < 0.001$), which persisted after controlling for child age and maternal education (proxy for socioeconomic status). Children with OB, but not HW, showed an increase in WS in block 5 relative to block 1. Further, a maternal BMI by child weight status interaction showed that as maternal BMI increased, WS decreased for children with HW but not OB ($p < 0.05$). This effect was no longer significant after controlling for maternal education. There were no effects of child or maternal weight status on net score or LS. Results show that children with OB may adapt behavior based on positive outcomes differently than children with HW, and maternal BMI may moderate the use of positive outcomes in decisions. These differences in decision making may inform the development of interventions to improve maladaptive eating behaviors.

P31 **Psychometric Properties Of The Child Eating Behavior Questionnaire In Children With Overweight/ Obesity: A Unitary Factor Structure**

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Children with obesity make up 18.5% of the U.S. population (Hales, Carroll, Fryar, Ogden, 2017). Despite this growing public health problem, few assessments of eating behaviors have been developed in children. The Child Eating Behavior Questionnaire (CEBQ) was developed to evaluate appetitive characteristics among children; however, analyses of the psychometric properties of the CEBQ have yielded differing factor structures, in addition to having been conducted primarily in samples of young children of healthy weight. This study aims to evaluate the psychometric properties of this widely used measure in a treatment seeking sample of school age children with overweight and obesity. The sample was comprised of 140 children (BMIZ= 1.94 (0.37); mean age = 10.64 (1.59), 68% Female; 66% White; 26% Hispanic) and their parent (BMI= 29.35 (6.45); mean age = 43.64 (6.63); 89% female; 69% White; 19% Hispanic; 57% income >$100,000/ year) who completed an abridged version of the CEBQ. Children's eating behaviors were reported across five domains: food responsiveness, enjoyment of food, emotional over-eating, slowness in eating, and satiety responsiveness, in line with previous studies that have selected only relevant domains for analysis (Carnell & Wardle, 2007). Exploratory factor analysis (EFA) was performed, with parallel analysis and optimal coordinates suggesting three eating domains to be retained, while the acceleration factor suggesting one factor be retained. More sophisticated hierarchical bi-factor modeling suggests a unitary construct accounts for a majority of the reliable variance. In sum, all analytic approaches suggest fewer than five domains be retained, with a more rigorous approach suggesting subscales are best subsumed under a unitary construct.

P32 **Importance Of Forebrain Angiotensinergic Mechanisms For Sodium Intake Induced By Different Stimuli**

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In addition to angiotensin II (ANG II) and aldosterone that are typical facilitatory stimuli for sodium appetite, surprisingly, hypertonic NaCl intake was also found in hyperosmotic rats or rats with central cholinergic activation if the inhibitory mechanisms of the lateral parabrachial nucleus (LPBN) are deactivated. In the present study, we tested the effects of the blockade of central angiotensinergic AT1 or muscarinic receptors on water and NaCl intake when the inhibitory mechanisms are deactivated with injections of moxonidine (alpha2-adrenoceptor/imidazoline agonist) into the LPBN in rats treated with ANG II or carbachol (cholinergic agonist) intracerebroventricularly (icv) or 2 M NaCl (2 ml) intragastrically. Male Holtzman rats (290-310 g, n = 9-10/group) with stainless steel cannulas implanted in the lateral ventricle and LPBN were used. LPBN injection of moxonidine (0.5 nmol) increased water and 0.3 M NaCl intake in rats treated with ANG II (50 ng) or carbachol (4 nmol) icv or 2 M NaCl intragastrically (2 ml/rat). Previous icv injection of losartan (AT_1 antagonist, 100 μg) abolished water and 0.3 M NaCl intake in rats treated with carbachol icv or 2 M NaCl intragastrically combined with moxonidine into the LPBN. Atropine (muscarinic antagonist, 20 nmol) also abolished water and 0.3 M NaCl intake in rats treated with 2 M NaCl combined with moxonidine into the

LPBN. However, atropine did not change 0.3 M NaCl intake induced by icv ANG II combined with moxonidine into the LPBN. The results suggest that the activation of forebrain angiotensinergic mechanisms is crucial for sodium intake induced by different stimuli, including hyperosmolarity and central cholinergic activation, when LPBN inhibitory mechanisms are deactivated.

P33 **Testing The Role Of The Mas Receptor In The Anti-Dipsogenic And Anti-Natriorexigenic Effects Of Estradiol.**

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Estradiol (E2) inhibits fluid intake stimulated by the hormone angiotensin II (AngII). While multiple mechanistic studies have tested for interactions between E2 and the angiotensin type 1 receptor, no studies have examined interactions between E2 and the Mas receptor (Mas-R). The Mas-R is part of the protective arm of the AngII signaling pathway because it is associated with antihypertensive effects. Importantly, E2 protects against hypertension through regulation of Mas-R signaling. The goal of this study, therefore, was to examine the role of the Mas-R in regulating E2's inhibitory effect on drinking. Ovariectomized female rats (n = 10) were implanted with a ventricular cannula attached to a chronic minipump delivering either ACSF (control) or 20 μg/day A-799 (Mas-R antagonist). After recovery, rats were treated with oil or 10 μg estradiol benzoate (EB) once a day for two days. Twenty-four hours after the second treatment, water was removed from the cages. The next day (24 h later) water was returned and 2 h intake was recorded. This was repeated the next week, with rats receiving the opposite hormone treatment. Rats then had access to both water and 1.5% saline and the two-week protocol was repeated. Preliminary data suggest that EB decreased both water and saline intake regardless of drug treatment. Daily fluid intake and body weights were also measured throughout the experiment. There was no effect of A-799-treatment on daily fluid intake or body weight gain. When A-799-treated rats received EB-treatment, however, they lost more weight compared to control EB-treated rats, p = 0.06. These preliminary results suggest that the Mas-R is not involved in mediating the anti-dipsogenic responses of estradiol but may be involved in E2's inhibitory effect on body weight.

P34 **Is Salt Appetite Related To Sodium Sweat Loss In Athletes, And Does It Increase Their Dietary Sodium Intake**

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Understanding the determinants of salt intake may be useful in establishing strategies for sodium regulation, a public health concern. Many athletes use sodium supplementation as advised by athletic associations. It is not known if the use of sodium by athletes exceeds that of the general population, whether its use during training and competition increases dietary intake of sodium, nor whether any increase in sodium intake is driven by cognition, conditioning, or physiology. Accordingly, in a group of competitive runners (>4x40 min/week exercise) and sedentary controls (< 60 min/week exercise), we examine dietary sodium intake and preference by FFQ and spot urine. In addition, we test changes in sodium preference related to acute athletic exertion, varied by temperature, a determinant of sweat and resultant sodium loss. In our lab, athletes meeting inclusion criteria ran at 10% below their predetermined anaerobic threshold for 30 min treadmill at ~ 18^{o}C or ~28^{o}C a week apart. Physiological measures, performance, and exertion were monitored. We now have data for n=13/30 runners, and 5/30 controls. Partial results confirm the efficacy of the environmental manipulation on physiological and perceived measures of exertion, which are significantly increased by temperature, as is sweating and sodium loss (69.5±10.1 vs 98.7±9.6, mmol Na^{+}±SE, p=.0002). However, sodium taste preference was not altered by running, or environmental temperature, with this size sample. FFQ is being analyzed. Updated results and cautionary conclusions will be reported in July. Results may also be of value for individual athletic participants, providing information of their sodium loss in exercise, dietary analysis, etc, which can be of value for performance and recovery.

P35 **Mild Water Restriction Of Female Rats Does Not Impact Estrous Cycle Stability.**

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Before effects of hormone-level changes across the estrous cycle on feeding and taste-guided behaviors can be assessed, it should be determined if the water restriction necessary to motivate rats in tasks influences the estrous cycle. The present study examined if mild water restriction akin to that used in behavioral tasks would destabilize the estrous cycling of female rats. We used 24 Sprague-Dawley female rats from 12 litters across 2 study phases in an A-B-A between-subjects design. Sister-pairs of rats were divided into two experimental groups, one of which was never water restricted and one of which was restricted to 10 ml of water per day, Monday through Friday, during the B phase of the experiment; all animals received ad libitum access to water during the two 3-week A phases and over the weekends during the 3-week B phase. The estrous cycles of all the rats were tracked every week day and were defined by 2 observers blind to the experimental group via microscopic analysis of stained cells collected via vaginal swab. Five-day cycle periods were scored in a binary fashion as either stable or not, with an unstable cycle period defined as 3 or more consecutive days of a single stage. Independent t-tests revealed no significant differences in the percent of rats presenting with unstable cycles overall and for each 3-week phase between experimental groups (water-replete vs. water-restricted). This

suggests that water restriction has no direct effect on estrous stability in rats, and that mild water restriction can be used as motivation in behavioral tests in female rats without overt impact on the estrous cycle.

P36 **Oxytocinergic Neurons In The Paraventricular Nucleus Of The Hypothalamus Are Potent Mediators Of Sodium Intake And Anxiety-Like Behavior**

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Central oxytocin (OT) regulates ingestive behavior and mood; however, the circuits mediating these effects are unclear. Here, we use genetically-modified mice with *in vivo* optogenetics to evaluate fluid intake and anxiety-like behavior during selective excitation or inhibition of OT neurons in the paraventricular nucleus of the hypothalamus (PVN). Male mice with the expression of Cre recombinase directed to the OT gene were used in two ways: (i) They were bred to express an excitatory opsin (ChR2) in OT neurons; (ii) They were injected bilaterally into the PVN with adeno-associated viruses that synthesize either an inhibitory opsin (Switch), or enhanced yellow fluorescent protein (eYFP). Mice were implanted with fiber optics targeting the PVN and behavioral responses to blue light-induced stimulation or inhibition were examined. In response to blue light stimulation (20Hz, 20ms), there was no significant difference in water intake, based on the number of licks, between OT-ChR2 mice and their controls. However, the OT-ChR2 mice exhibited a significant reduction in NaCl intake compared to their controls [33±2 and 88±18 licks ($p< 0.001$), respectively]. In OT-Switch mice, blue light stimulation (0.03Hz, 500ms) also elicited no significant differences in water intake compared to eYFP mice. Strikingly, the OT-Switch mice showed a substantial increase in NaCl intake compared to their eYFP controls [105±19 and 30±9 licks ($p< 0.001$), respectively]. When tested for anxiety-like behavior in the elevated plus maze, the OT-Switch mice spent more time in the closed arms compared to their eYFP controls which moved freely in both closed and open arms ($p< 0.05$). Our results indicate a direct involvement of OT PVN neurons in the control of fluid intake and anxiety-like behavior.

P37 **High-Salt Diet Does Not Cause Obesity In C57Bl/6J Mice**

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Epidemiological studies demonstrate that salt intake and body weight are positively associated but is this a causative relationship? To investigate, we fed ten groups of 12 adult female C57BL/6J mice diets based on either the AIN-76A formulation (3.8 kcal/g) or a high-energy version of this formulation (4.6 kcal/g); each diet was provided at five concentrations of sodium (0.15, 0.26, 0.47,0.84, 1.49 mg/kcal). Over 18 weeks, dietary salt did not affect the food intakes or body weights of mice fed the 3.8 kcal/g diets. However, it significantly reduced the body weights of mice fed the 4.6 kcal/g diets. Next, we tested the hypothesis that thirst produced by consuming salt stimulates sugar-sweetened beverage consumption, leading to obesity. Four groups of 12 adult male C57BL/6J mice were fed a modified AIN-76A low-salt diet (0.15 mg/kcal) or a high-salt diet (1.49 mg/kcal). All mice could drink water *ad libitum*, and half also could drink 16% sucrose solution. Body weights and food, water, and sucrose intakes were monitored for 8 weeks. Contrary to the hypothesis, high dietary salt did not stimulate sucrose intake. Overall, these experiments do not support the hypothesis that salt consumption causes obesity. Salt is an incidental ingredient of many high-fat and high-energy foods, that promote obesity; thus salt consumption may be incidental to the consumption of other ingredients that render individuals obese.

P38 **Leptin&Rsquo;S Action On Glp-1 Neurons Is Not Sufficient To Restore Food Intake And Anxiety-Like Behavior In Leptin Receptor-Deficient Mice**

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The nucleus of the solitary tract (NTS) is critical for central integration of signals from visceral organs. Preproglucagon (PPG) neurons in the NTS produce glucagon-like peptide-1 (GLP-1) and send direct projections to the paraventricular nucleus of the hypothalamus (PVH). Nearly all PPG neurons coexpress leptin receptors and are directly responsive to leptin. Leptin functions during development to organize hypothalamic metabolic circuitry, but its role in specifying patterns of brainstem-hypothalamic connections is unknown. To determine if leptin is required for development of PVH GLP-1 projections, we used PPG-cre mice to target a fusion protein of synaptophysin and tdTomato to PPG neurons in order to visualize neuronal projections in leptin-deficient $Lep^{ob/ob}$ mice. In contrast to development of AgRP projections to the PVH, projections from PPG neurons show an increase in $Lep^{ob/ob}$ mice compared with controls. The physiological impact of these developmental events was evaluated in $LepRb^{TB}$ mice, which are functionally null for LepRb. LepRb expression was restored specifically in PPG neurons by crossing $LepRb^{TB}$ and PPG-cre mice, resulting in mice with LepRb signaling restored in PPG neurons on an otherwise null LepRb background. Because PPG neurons regulate metabolic function and stress responses, we measured latency to eat in a novelty induced hypophagia test, as well as amount consumed in a stress-induced feeding test. Meal patterns and performance on anxiety-like paradigms were also tested. Surprisingly, mice with LepRb restored on PPG neurons did not perform differently than mice

with global leptin receptor deficiency, indicating leptin action on GLP-1 neurons alone is not sufficient to normalize food intake and stress responses under the conditions tested.

P39 **The Effects Of Leptin Mutations And Diet-Induced Obesity On Glucose Homeostasis In The Zebrafish**

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Leptin is classically thought to be an adipostatic signal communicating information from the adipose tissue to the brain, thereby regulating energy intake and expenditure. Recently, it has been demonstrated that in the zebrafish (*Danio rerio*), contrary to humans and other mammals, leptin does not regulate adipostasis but glucose homeostasis. From an evolutionary perspective, this suggests that a role for leptin in regulation of glucose homeostasis is conserved across vertebrates, whereas its role as an adipostatic factor is likely to be a secondary role acquired by mammals over the course of evolution. Moreover, due to a fish-specific third whole genome duplication event, zebrafish have two leptin variants: -a and -b. The specific functions of these paralogues are yet to be fully elucidated. In the current study, we utilized the CRISPR/Cas9 system to generate knockout mutant zebrafish for both leptin-a and leptin-b, and for the leptin receptor. 3-month old male mutant fish and wild type control fish were then exposed to either an 8-week long overfeeding regime, consisting of 6 daily feeds, or a standard diet of 1 feed per day. One feed consisted of 20 mg/fish of ZM-400© fish pellets. Food intake was monitored during and after every feed. Body weights were measured weekly. Glucose tolerance tests were performed to assess changes in glucose homeostasis at the beginning and the end of the 8-week period. Finally, half the fish were treated with metformin for 7 days (20μM, dissolved in tank water, solution changed daily) in the final week of the 8-week period to investigate whether impaired glucose homeostasis could be ameliorated. Collectively, these data provide new insight into the interplay between leptin and glucose homeostasis.

P40 **Endocrine Cephalic Phase Responses To Food Cues &Ndash; Weighing The Evidence**

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Cephalic phase responses (CPRs) are anticipatory and conditioned neural mediated responses to food cues. CPRs occur before nutrient absorption and are thought to play a role in satiation and glucose homeostasis. Cephalic insulin and pancreatic polypeptide (PP) responses have been extensively studied, but contrary to animal work findings in humans are inconsistent. Therefore, we performed a systematic review of studies done in humans to determine the conditions under which cephalic insulin and PP responses occur, together with their magnitude and time of onset. Initially, 582 original research papers were found. After title and abstract screening, 130 papers were found eligible and two observers screened full text. Eventually, 50 publications were included for analysis. A cephalic insulin increase (>1 µIU/mL) was observed in 48 of the 124 treatments, 26 (21 %) of these responses were statistically significant. A median(IQR) insulin increase of 2.5(1.6-4.5) µIU/mL was found at 5±3 min after the food cue. A cephalic PP increase (>10 pg/mL) was found in 20 out of the 39 treatments, 9 (23 %) of these were significant. A median(IQR) PP increase of 99(26-156) pg/mL from baseline was found 9±4 min after food cue onset. In conclusion, CPRs are relatively small and show substantial variation between food cues and individuals, both in magnitude and onset time. Therefore the biological relevance of cephalic insulin and pancreatic polypeptide responses are debatable and their role in satiation and glucose homeostasis should be questioned.

P41 **Peptide Yy Mediates The Satiety Effects Of The Short Chain Fatty Acid - Butyrate**

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The gut hormone Peptide-YY (PYY) plays an important role in regulating food intake. Fermentation of prebiotic fiber by gut microbiota produces short-chain fatty acids (SCFA), such as butyrate, which in turn decrease food intake and promote weight loss in rodent models. SCFA have been shown to enhance PYY secretion. However, whether PYY is causative to SCFA-induced changes in energy balance is unknown. Our objectives were to determine the dose-response effects of butyrate on energy balance, and assess whether PYY signaling is essential for mediating the satiety effects of butyrate. **Methods:** Male Sprague Dawley rats were randomized to isocaloric high-fat (40% kcal, 4.63 kcal/g) diets: 1) control (0% sodium butyrate, n=14), 2) 5% sodium butyrate (n=13), or 3) 10% sodium butyrate (n=12), and followed for upto 4 weeks. A PYY Y-2 receptor antagonist (BIIE0246) or vehicle were administered IP during the first week of the study. **Results:** Compared to control, 10% butyrate decreased food intake and respiratory quotient for 4 days, whereas, 5% butyrate was ineffective. Notably, after 2 weeks, 10% butyrate decreased body weight and fat gain than control, but without altering energy expenditure. Importantly, systemic Y-2 receptor blockade stimulated food intake by ~50% for 1h and increased respiratory quotient, without altering energy expenditure, only in 10% butyrate group. **Conclusions:** Dietary butyrate dose-dependently decreased food intake, respiratory quotient and adiposity. Importantly, Y-2 receptor blockade attenuated butyrate-induced hypophagia, supporting a role for endogenous PYY in mediating the satiety effects of butyrate.

P42 **Time Of Day-Dependent Action Of Hypothalamic Leptin Signalling**

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Synchronisation between biological clocks and metabolism is crucial for the survival of most species. Here, we investigated whether leptin signalling is regulated in a daily manner in the hypothalamus of mice. Therefore, we examined the ability of leptin to induce leptin signalling in the arcuate nucleus of fasted mice throughout the 24-h rhythm. By measuring activated phospho-STAT3-immunoreactive cells after leptin injection, we found that leptin sensitivity was regulated in a rhythmic manner in control mice. In these mice leptin sensitivity was highest at Zeitgeber time (ZT) 0, with sensitivity declining throughout the light phase and increasing throughout the dark phase. Surprisingly, leptin resistance in mice fed a high-fat diet (HFD) was not universal, but varied during the day, with deteriorated leptin signalling occurring only during the last half of the dark phase and the first half of the light phase compared with control mice. At all other time points, leptin sensitivity was similar to control mice. We next injected leptin or vehicle in control and HFD mice either at ZT0 or ZT12 and compared their caloric intake. Surprisingly, control mice showed decreased caloric intake only when leptin injections occurred at ZT0, while HFD mice remained resistant to leptin at both ZT0 and ZT12, suggesting that at the behavioural level, control mice are sensitive to exogenous leptin exclusively during the first part of the light phase. Furthermore, in control and HFD *ad libitum* fed mice caloric intake was identical during the day, except for elevated caloric intake in HFD mice between ZT21-3, the period when these mice were leptin resistant. These data provide evidence that daily rhythms play a crucial role in the control of leptin action and whole body energy homeostasis.

P43 **Activation Of Leptin Receptor-Expressing Neurons In Lateral Hypothalamus Enhances Appetitive Behavior In Mice**

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The symptom of eating disorders that is difficult to treat is a dissociation between food-seeking behavior and metabolic needs. The lateral hypothalamus (LHA) regulates various motivated behaviors including food intake, and among many neuronal populations inside, LHA GABAergic neurons are known to be involved in modulation of food reward and consumption. Previous studies showed that activation of LHA GABAergic neurons enhance food intake and compulsive behaviors in mice. However, specified behavioral phenotypes and functions of the subset of LHA GABAergic neurons are unclear. Thus, our research aimed to identify the food-related behavioral phenotypes that are regulated by leptin receptor-expressing neurons in LHA. We performed food-seeking test, operant contioning chamber test, overall chow and palatable food intake test and marble burying test. Interestingly, through behavior assays, we found that chemogenetic activation/inhibition of LHA leptin receptor neurons only modulate 'food-seeking' behavior without altering food intake. However, activation of LHA GABAergic neurons increased both food intake and compulsive behaviors without affecting food-seeking. These results suggest that food-seeking is independent from food intake, and LHA leptin receptor expressing neurons are specifically involved in food-seeking behavior that can be targeted to treat eating disorders.

P44 **Cortical Inputs To The Lateral Hypothalamus Influence Body Weight And Food Choice**

RACHEL E CLARKE, MOYRA B LEMUS, SARAH H LOCKIE, ZANE B ANDREWS
Monash University, Clayton, Australia

Food choices are influenced by both metabolic need and hedonic motivation. The lateral hypothalamus (LH) is uniquely positioned to receive information related to both internal metabolic status and external cues. How the LH balances homeostatic and hedonic inputs to coordinate feeding and motivated behaviour has not yet been fully elucidated. The cortical regions of the brain including the medial pre-frontal cortex (mPFC) and the anterior cingulate cortex (ACC) are understood to be involved in decision-making processes surrounding food and food reward. Anatomical tracing studies demonstrate monosynaptic projections from the mPFC and ACC to the LH. This study aims to investigate whether these circuits are functionally relevant to feeding and motivated behaviours. A dual-viral transgenic approach (Cav2-cre GFP delivered to LH, AAV-FLEX-taCaspase3 delivered to mPFC or ACC) was used to ablate mPFC-LH and ACC-LH pathways in separate cohorts of C57BL/6 mice. All animal experiments were conducted in line with Monash Animal Ethics requirements. Ablation of the mPFC-LH pathway resulted in increased bodyweight on a chow diet ($p=0.033$, n=12 experimental, n=13 control). While ablation of the ACC-LH pathway resulted increased bodyweight on a high fat diet (HFD) ($p=0.013$, n=12 experimental, n=13 control). A battery of behavioural tests were used to investigate a potential role for this circuit in anxiety, risk-reward processing and hedonic aspects of feeding. Mice with mPFC-LH pathway ablation tended to consume more HFD than controls over three-days of *ad lib* access to both chow and HFD ($p=0.049$, n=12 experimental, n=11 control). Results so far suggest these cortical-LH pathways influence food choices and body weight.

Thursday, July 11, 2019

8:30 - 10:30 AM	Progress
SYMPOSIUM 2: Health Benefits of Time- Restricted Feeding	

Chair(s): Christine Feinle-Bisset

8:30 **Intermittent Fasting Strategies To Optimise Metabolic Health In Men And Women With Obesity.**

LEONIE HEILBRONN[1,2]

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Calorie restriction (CR) is a powerful tool to prevent or delay chronic disease, promote healthy aging and increase lifespan in preclinical models. Intermittent fasting (IF) is an alternative strategy that switches fasting with periods where food is freely available. IF has pleiotropic metabolic benefit to promote repair mechanisms, stress resistance, optimise energy utilisation and increase lifespan in preclinical models. Time restricted eating (TRE) is a novel tool that simply limits food intake to discrete time periods daily (eg 8-10 hours). TRE resets peripheral clocks and prevents the metabolic consequences of high fat diet in mouse. Our recent work has compared the effects of 1 week TRE with and without a phase delay on glycaemic control and gastrointestinal (GI) hormone release in men at risk of type 2 diabetes, and has examined the effects of IF provided in matched energy restriction to daily CR and vs IF prescribed in energy balance in women with obesity. We have shown that IF was superior to CR when food was prescribed at matched energy restriction, but did not differentially improve health when prescribed in energy balance, and transiently induced insulin resistance. TRE on the other hand had minimal impact on body weight but substantially improved glucose control in men. There was no effect of TRE on the GI hormone release to a test meal. New studies are underway to better understand the circadian impacts and optimal feeding and fasting cycle to maximise glucose control and metabolic health in men and women at risk of t 2 diabetes .

9:00 **Health Benefit Of Time-Restricted Feeding**

ERIC RAVUSSIN[1], COURTNEY PETERSON[1,2]

[1]Pennington Biomedical, Baton Rouge, LA, United States, [2]UAB, Birmingham, AL, United States

Caloric restriction has been the favored dietary intervention for weight management and improvement of metabolic health in humans. Recently, novel feeding interventions first developed in rodents have been implemented in human RCTs. Intermittent fasting (IF) represents a broad class of meal timing interventions that involve alternating periods of eating and extended fasting. Such interventions have been found to reduce body weight, improve cardiometabolic health, reduce some forms of cancers, slow down the progression of auto-immune disease and finally improve biomarkers of aging. However, emerging evidence suggests that not all forms of IF such as alternate day fast or alternate day modified fast may be superior to continuous daily energy restriction in humans. One novel form of IF called time-restricted feeding (TRF) appears to improve adherence to IF and especially improve cardiometabolic health in people. TRF involves eating within < 10-hour daily period and fasting for the remainder of the day. More than 30 studies in rodents and approximately 10 pilot-sized studies in humans have found that TRF reduces body weight and hunger, improves insulin sensitivity, lowers blood pressure, reduces inflammation and oxidative stress, improves circadian rhythms, and/or extends lifespan (rodents). We recently showed that TRF has intrinsic cardiometabolic benefits independent of energy restriction in humans. Importantly, we found that although TRF does not affect 24-hour energy expenditure in humans, it does reduce the desire to eat and ghrelin levels, and enhance 24-hour fat oxidation and metabolic flexibility. With feasibility data demonstrating reasonably high adherence rates, TRF is a promising ingestive behavior strategy to improve weight control and cardiometabolic health.

9:30 **Time Restricted Feeding And Peripheral Appetite Regulation.**

AMANDA J PAGE[1,2]

[1]Vagal Afferent Research Group, Adelaide Medical School, University of Adelaide, Adelaide, Australia, [2]Nutrition, Diabetes and Metabolism, Lifelong Health, South Australian Health and Medical Research Institute (SAHMRI), Adelaide, Australia

Diurnal rhythms increase energy efficiency by temporally separating incompatible metabolic processes, such as anabolism and catabolism. Disruption of this rhythmicity can have significant health implications. For example, shift workers are at higher risk of being obese than individuals working ‘normal’ hours. Diurnal rhythms within the periphery are under the control of the suprachiasmatic nucleus, however, they also respond to other cues such as food intake. Therefore, the timing of food intake may play a critical role in the regulation of many peripheral processes. The gut-brain axis plays a major role in food intake regulation. It relays information, about the quantity and nutrient composition of food consumed, to the brain where it is integrated with other signals to regulate subsequent food intake. Vagal afferent sensory nerves are an important conduit for the transmission of

these signals and display a high degree of plasticity. For example, gastric vagal afferent (GVA) responses to food related stimuli display diurnal rhythms, presumably to finely match food intake to energy requirements. However, in high fat diet-induced obese mice or mice exposed to simulated shift work conditions, diurnal rhythms in GVA signals are lost. It is known that changes in vagal afferent signalling, observed after chronic high fat diet feeding, are resistant to reversal upon return to a normal diet. However, recent data indicate diurnal rhythms in GVA responses to food related stimuli can be entrained by food intake. Further, the loss of diurnal rhythmicity, observed in chronic high fat diet conditions, can be prevented by time restricted feeding. This data provides support for time restricted feeding regimes in the treatment of obesity and management of weight loss.

10:00 **Counting Hours Not Calories: Time-Restricted Feeding As A Therapeutic Strategy For Pleiotropic Cardiometabolic Benefits**

AMANDINE CHAIX[1], TERRY LIN[1], HIEP D LE[1], MAX W CHANG[2], EMILY MANOOGIAN[1], SATCHIDANANDA PANDA[1]

[1]The Salk Institute for Biological Studies, La Jolla, CA, United States, [2]Department of Medicine, University of California San Diego, La Jolla, CA, United States

Diet and exercise come to the forefront in the treatment and/or prevention of nutrition-related chronic disease. These strategies have had limited success due to the difficulty of maintaining the required lifestyle changes over long time period. As a result, there has been an explosion in new dieting strategies such as intermittent fasting, fasting mimicking diets, and time-restricted feeding (TRF). TRF recommends daily caloric intake to be limited **in time** independently of caloric content. TRF rose from the observation that mouse models of diet-induced obesity have disrupted daily eating patterns and altered daily rhythms in the expression of metabolic and circadian clock genes. This suggested that the daily timing of food intake and the circadian clock could contribute to the pathophysiology of metabolic disease. We show that TRF can prevent and reverse cardiometabolic disorders under various nutritional stresses and protect clock-deficient mice from metabolic disease. Recent evidence suggests that TRF can also lead to weight loss and cardiometabolic benefits in humans. Our results demonstrate that the temporal pattern of food intake plays a key role in nutritional balance.

10:30 - 12:30 PM	Progress
ORAL SESSION 2: Vagal-Hindbrain Control of Feeding	

Chair(s): Suzanne Appleyard and Daniel Brierley

10:30 **(Nita Award Winner) Regulation Of Food Intake By Astrocytes In The Brainstem Dorsal Vagal Complex**

ALASTAIR J MACDONALD[1,2], FIONA E HOLMES[2], CRAIG BEALL[1], ANTHONY E PICKERING[2,3], KATE L J ELLACOTT[1]

[1]Institute of Biomedical and Clinical Science, Medical School, University of Exeter, Exeter, United Kingdom, [2]School of Physiology, Pharmacology and Neuroscience, University of Bristol, Bristol, United Kingdom, [3]Anaesthesia, Pain and Critical Care Sciences, Translational Health Sciences, Medical School, University of Bristol, Bristol, United Kingdom

A role for glial cells in brain circuits controlling feeding has begun to be investigated with modulation of hypothalamic astrocyte signaling implicated in regulating energy homeostasis. Neurons in the brainstem nucleus of the solitary tract (NTS) integrate information from the periphery, signal visceral stimuli to the CNS, and regulate food intake. We hypothesized that astrocytes in this nucleus can also respond to, and influence, food intake. Mice fed a high-fat chow for 12 hours during the dark-phase showed NTS astrocyte activation, measured by an increase in the number (65%) and morphological complexity of glial-fibrillary acidic protein (GFAP)-immunoreactive cells adjacent to the area postrema (AP), compared to control chow fed mice. To measure the impact of astrocyte activation on food intake we delivered designer receptors exclusively activated by designer drugs (DREADDs) to astrocytes of the dorsal vagal complex (DVC; encompassing NTS, AP and dorsal motor nucleus of the vagus) using an adeno-associated viral (AAV) vector (AAV-GFAP-hM3Dq_mCherry). Stimulation of these receptors with clozapine-N-oxide (CNO; 0.3mg/kg) reduced dark-phase feeding by 84% at 4 hours post-injection when compared with saline-injected trials. DREADD-mediated activation of DVC astrocytes also reduced refeeding after an overnight fast when compared to AAV-GFAP-mCherry expressing control mice (71% lower, 4 hours post-injection). CNO injection did not cause conditioned place avoidance. The pattern of c-FOS immunoreactivity induced by CNO injection showed the activation of neighboring neuronal feeding circuits. This strongly suggests that NTS astrocytes respond to acute nutritional excess, are involved in the integration of peripheral satiety signals and can reduce food intake when activated.

10:45 **Noradrenergic Neurons In The Nucleus Of The Solitary Tract Control Food Intake**

ZHI YI ONG[1], HARVEY J GRILL[2], GAVAN P MCNALLY[1]

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

The lack of effective long term treatments for obesity calls for better understanding of the neural mechanisms that regulate food intake. We focus on hindbrain neurons as they are a critical hub for the integration of peripheral and central signals in food intake control. The noradrenergic neurons in the nucleus of the solitary tract (NTS) are of interest because these neurons are activated by satiation signals and appetite-suppressing peptides including leptin and cholecystokinin, suggesting a role for these neurons in food intake control. However, the function(s) of NTS noradrenergic neurons are not well-characterised. This study aims to examine the role of NTS noradrenergic neurons in food intake control. To target and manipulate NTS noradrenergic neurons, we used transgenic TH-Cre rats coupled with chemogenetics (excitatory hM3Dq) and examined the function of these neurons in a battery of feeding behavioural tasks. Results showed that chemogenetic activation of NTS noradrenergic neurons reduced chow and high-fat diet intake, and suppressed deprivation-induced feeding. Activation of these neurons also reduced the motivation to work for sucrose, blocked a place preference for high-fat food and prevented cue-elicited food approach behaviours. These effects were not observed in reporter control rats that do not express hM3Dq. Furthermore, activation of NTS noradrenergic neurons did not induce malaise, affect locomotor activity, or increase anxiety. Together, we showed that NTS noradrenergic neurons are not only involved in energy state-driven control of food intake but also in food reward. Importantly, the intake inhibitory effects of NTS noradrenergic neurons are not secondary to malaise, motor impairments or anxiety.

11:00 **A Full Brain: Brain(Stem) Responses To Tasting Chocolate Milk Over The Course Of Satiation**

MARLOU P LASSCHUIJT[1], MONICA MARS[1], CEES DE GRAAF[1], PAUL A. M. SMEETS[1,2]

[1]Division of Human Nutrition and health, Wageningen, Netherlands, [2]Image Sciences Institute, Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht, Netherlands

Satiation develops from the integration of taste and gastric signals in the brainstem and hypothalamus. However, the transition from a hungry to a sated state and the role of the brainstem in this process is poorly understood. The aim of this study was to determine differences in brain(stem) responses to sweet taste over the process of becoming satiated. Forty, right-handed subjects (17M/23F, 24±3 y, BMI 22±2 kg/m2) participated in a repeated-measures experiment. Stomach filling and brain responses to sips of neutral taste stimuli and high and low sweet chocolate milk were measured in a hungry, a 50% and a 100% sated state using (f)MRI. To induce satiety, subjects drank chocolate milk between blocks. To assess brainstem activation we corrected for cardiac (ECG) and respiratory noise using the PhysIO Toolbox. Preliminary analysis (n=7) showed parabrachial nucleus (PBN), and nucleus tractus solitarius (NTS) activation upon flavor and sweet taste (high>low) perception, respectively. In the 100% satiated compared to the hungry state; increased taste-related brain activation was found in the

insula, orbitofrontal cortex (OFC) and putamen. Taste-related activation in the thalamus decreased over the course of satiation also after correcting for stomach distention. To conclude, we detected PBN and NTS responses to flavor and sweet taste. Taste-related activation seemed to be modulated by satiation in the insula, OFC, putamen and thalamus. Further analyses are ongoing to determine how brainstem nuclei and higher sensory and reward areas are involved in the process of satiation.

11:15 **(Nita Award Winner) Going With Your Gut: Tvns Increases Invigoration For Food Rewards**

MONJA P. NEUSER[1], VANESSA TECKENTRUP[1], MARTIN WALTER[1,2,3], NILS B. KROEMER[1]

[1]Eberhard Karls University Tübingen, Department of Psychiatry and Psychotherapy, Tübingen, Germany, [2]Otto-von-Guericke University Magdeburg, Department of Psychiatry and Psychotherapy, Magdeburg, Germany, [3]Leibniz Institute for Neurobiology, Magdeburg, Germany

Energy intake exceeding individual demands is central to the development of overweight and might be mediated by maladaptive regulation of metabolic processes, including motivated behavior. The vagus nerve modulates dopaminergic signaling and homeostatic control via projections to the nucleus tractus solitarii (NTS). While vagus nerve stimulation (VNS) has been effectively applied to promote weight loss in both, preclinical settings and in humans, its acute effects on motivated behavior remain inconclusive. To examine how vagal metabolic signaling acutely modulates motivation, we applied transcutaneous VNS (or sham) to 41 healthy, overnight-fasting participants. They completed two sessions of an effort allocation task (EAT) in a randomized crossover design. In the task, participants had to exert effort (i.e., normalized button-press frequency; costs) to earn rewards (money or food) of low or high magnitude. Overall, higher reward magnitude increased the invigoration of work, $t = 4.544$, $p < .001$, and tVNS further increased the invigoration for food rewards, $t = 2.965$, $p = .005$. Critically, behavioral invigoration declined less steeply with decreases in self-reported wanting ($\Delta bs = -.11$, $ps \leq .026$), indicating reduced discounting of the utility to work for food reward under tVNS. However, tVNS did not increase effort in general or vigor for monetary rewards suggesting specificity of stimulation effects. To summarize, we found that tVNS facilitated invigoration for food rewards. This could be explained by an increase in incentive value conferred by food rewards. We conclude that metabolic signaling via tVNS can acutely increase motivation for food which might be a useful intervention to reduce reward deficiency.

11:30 **Utilizing A Novel Cart-Cre Mouse To Study Gut-Brain Signaling**

ALAN ARAUJO, ARASH SINGH, MOLLY MCDOUGLE, GUILLAUME DE LARTIGUE
University of Florida, Gainesville, FL, United States

Cocaine and amphetamine regulated transcript (CART) is an anorexigenic neuropeptide expressed in 40% of sensory neuron of the nodose ganglia (NG). The peripheral innervation of the NG^{CART} neruons, the metabolic stimuli that recruit them and the central neural circuits they engage remain unclear. We used a novel CART-Cre mouse line to address these questions. **Methods**: We validated a new CART-Cre mouse line by colocalizing cre-dependent tdTomato reporter with CART antibody in NG neurons. To map gut innervation of NG^{CART} neurons we injected cre-dependent viral constructs expressing YFP in the left and mCherry in the right NG of CART-Cre mice and performed 3D reconstruction of the tissue. To determine the metabolic stimuli that recruit NG^{CART} neurons, we performed two-photon imaging of nodose ganglia and recorded real time activity patterns in response to duodenal infusion of macronutrients (200ul) in CART-Cre mice crossed with GCAMP6S-flox mice. Finally we mapped the central projections of NG^{CART} neurons using a Cre-inducible, polysynaptic herpes simplex virus (H129ΔTK-TT) injected in right NG of CART-Cre mice. **Results:** tdTomato extensively co-localized with CART immunoreactivity in NG neurons. Both left and right NG^{CART} neurons innervate the length of the GI tract, but only the right NG innervates the villi. NG^{CART} neuron activity increased in response to intraduodenal infusion of intralipid (50%) and remained active for 20 minutes after infusion. Herpes-infected cells could be detected in numerous brain regions including the Substantia nigra, Ventral tegmental area, Central Amygdala, hypothalamus (PVH, DMH, ARC) and hippocampus. **Conclusion:** CART-Cre mice are a useful novel tool for studying gut-brain signaling.

11:45 **vAgal Afferent Ghrelin Signaling Promotes Episodic Memory And Influences Meal Patterns In Rats**

ELIZABETH A DAVIS[1], ANDREA N SUAREZ[1], CLARISSA M LIU[2], GUILLAUME DE LARTIGUE[3], SCOTT E KANOSKI[1,2]

[1]Human and Evolutionary Biology Section, Department of Biological Sciences, Dornsife College of Letters, Arts and Sciences, University of Southern California, Los Angeles, CA, United States, [2]Neuroscience Graduate Program, University of Southern California, Los Angeles, CA, United States, [3]Department of Pharmacodynamics, College of Pharmacy, University of Florida, Gainesville, FL, United States

Vagal afferent nerve (VAN) signaling sends sensory information from the gut to the brain, and while this pathway

is classically associated with meal size control, ablation of gut-originating VAN signaling also impairs hippocampal (HPC)-dependent episodic memory in rats. We hypothesized that ghrelin, a stomach-derived orexigenic hormone that communicates to its receptor (growth hormone secretagogue receptor [GHSR]) expressed on gut-innervating VAN terminals, is a key signaling molecule mediating VAN modulation of HPC memory function. To examine this hypothesis, adult male rats received bilateral nodose ganglion injections of an adeno-associated virus (AAV) expressing short hairpin RNAs targeting GHSR (or a scrambled control AAV) for RNA interference (RNAi)-mediated VAN GHSR knockdown. Results from behavioral analyses reveal that VAN-specific GSHR knockdown impairs episodic memory performance in a novel object in context task compared with controls. Given that impaired episodic memory in both humans and rodent models decreases the intermeal interval duration, we also hypothesized that knockdown of VAN GHSR would increase spontaneous meal frequency. Consistent with this hypothesis, meal-pattern analyses using automated food intake monitors revealed a significant increase in meal frequency in the VAN GHSR knockdown group compared with controls, coupled with a nonsignificant trend in reduced average meal size such that no significant differences were observed in cumulative 24h food intake. Collectively these results suggest that VAN GHSR signaling is important for encoding episodic elements of a meal-related memory, and chronic disruption of this pathway may lead to more frequent meal consumption.

12:00 **(Nita Award Winner) Pomc Projections From The Nucleus Tractus Solitarius To The Locus Coeruleus Control Food Intake**

SAMANTHA M FORTIN[1], JACK CHEN[1], RINZIN LHAMO[1], MATTHEW R HAYES[1,2]

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

The proopiomelanocortin (POMC) system plays an important role in regulating energy homeostasis, in part, through action of the POMC-derived peptide alpha-MSH on the neuroanatomically distributed melanocortin-4 receptor (MC4R). Here, we identify the locus coeruleus (LC), a nucleus of the pons implicated in arousal and autonomic regulation but overlooked in the context of energy balance control, as a novel site of MC4R activity-induced anorexia. Delivery of the MC4R agonist MTII to the LC acutely suppresses food intake and body weight in male and female mice. As injection of the retrograde tracer Fluoro-Gold into the LC reveals a direct projection to the LC from the nucleus tractus solitarius (NTS), one of two major sites of POMC neurons, we next examined the functional relevance of a POMC projection from the NTS to the LC. We utilized a Cre-dependent excitatory adeno-associated DREADD virus injected into the NTS of POMC-Cre mice to allow for selective stimulation of NTS POMC neurons with clozapine-N-oxide (CNO). We observed that delivery of CNO directly to the NTS POMC neuron terminals in the LC recapitulates the food intake and body weight-suppressive effects of systemic CNO delivery, providing evidence that the NTS POMC system suppress feeding behavior, in part, through projections to the LC. To further characterize this novel POMC projection, we are investigating the cellular phenotype of MC4R-expressing neurons within the LC. As the LC is a major source of noradrenaline in the brain and our fluorescent *in-situ* hybridization studies have revealed expression of the MC4R on noradrenergic neurons, ongoing studies are aimed at investigating the regulation of food intake by NTS POMC modulation of the LC noradrenaline system.

12:15 **Gut Projecting Vagal Efferent Motor Neurons Regulate Feeding Behavior**

ARASHDEEP SINGH[1], NICK DE WALT[2], MOLLY MCDOUGLE[1,2], ALAN DE ARAUJO[1,2], GUILLAUME DE LARTIGUE[1,2]

[1]Department of Pharmacodynamics, College of Pharmacy, University of Florida, Gainesville, FL, United States, [2]John B. Pierce Laboratory, Yale University, New Haven, CT, United States

Vagal efferent neurons (VEN) emerge from the dorsal motor nucleus of the vagus nerve (DMNV) to send top-down control of the gut function. Due to technical constraints, to date, the vast majority of data to understand changes in gastric tone and motility in rodents, and therefore the extent to which VEN control food intake remains unclear. **Methods:** To address this we employ a combinatorial viral approach to ablate VEN in freely behaving male Wistar rats (n=5). We first transfected the wall of stomach and duodenum of rats with a retrogradely transported adeno-associated virus carrying Cre (AAVrg-hSyn-BFP-Cre; 10^{13} PFU/ml). In this way, Cre recombinase was transported to VEN. Next, we injected the viral construct AAV-flex-ta-Casp3-TEVp, which induces Cre-dependent caspase expression bilaterally into the DMNV. Cumulative food intake and meal patterns were monitored using a BioDAQ feeding system in overnight fasted rats before, and 10 days after, VEN ablation. **Results:** $VEN^{upper\ GI}$ ablation with caspase reduced food intake by >50% within 4-hour of refeeding, compared to the same rats when non-ablated ($p< 0.005$). Reduced food intake in rats with $VEN^{upper\ GI}$ ablation was a consequence of smaller average meal size and shorter average meal duration ($p< 0.05$), with no significant reduction in meal number ($p=0.2$) and the latency to consume the first meal ($p= 0.2$). **Conclusion**: Gut projecting VEN play a role in the control of food intake.

10:30 - 12:30 PM	Mission 1
ORAL SESSION 3: Insulin, Glucose, and Diabetes	

Chair(s): Hubert Preissl and Lindsay Naef

10:30 **Oral L-Phenylalanine Stimulates Insulin And Glucagon-Like Peptide-1 (Glp-1), And Reduces The Plasma Glucose Response To A Mixed-Nutrient Drink, But Does Not Slow Gastric Emptying**

PENELOPE CE FITZGERALD, BENOIT MANOLIU, BENJAMIN HERBILLON, MICHAEL HOROWITZ, CHRISTINE FEINLE-BISSET
Adelaide Medical School, University of Adelaide, Adelaide, Australia

L-Phenylalanine (PHE), given orally at doses of ~10 g, stimulates plasma cholecystokinin (CCK) and reduces food intake; PHE also stimulates insulin and reduces the blood glucose response to a 25-g glucose load. Since CCK slows gastric emptying, which is a key regulator of postprandial blood glucose, we evaluated the effect of PHE on gastric emptying of, and the glycaemic responses to, a mixed-nutrient drink. 15 healthy men (age 23±1 y; BMI 22±1 kg/m^2) received on three separate occasions, in double-blind, randomised order, 10 g (PHE-10) or 5 g (PHE-5) PHE, or control (C), 30 min before a mixed-nutrient drink (400 kcal, 56 g carbohydrates). Plasma glucose, insulin and GLP-1 (n=13) were measured at baseline, in response to PHE (PHE alone), and for 2h following the drink. Gastric emptying of the drink was measured for 2h by ^{13}C-acetate breath test (n=14). PHE-10 and PHE-5 alone stimulated insulin compared with C (AUC, mU/L*min; PHE-10: 188±33, PHE-5: 181±34, C: 104±18; P< 0.05), but did not affect plasma glucose or GLP-1. In response to the drink, peak plasma glucose was modestly reduced after PHE-10 compared with C (mmol/L; PHE-10: 5.6±0.3, PHE-5: 5.9±0.2, C: 6.2±0.3; P< 0.05). There was no effect on insulin (AUC, mU/L*min; PHE-10: 3894±673, PHE-5: 4378±1339, C: 3595±658) or gastric emptying (% recovery of ^{13}CO2/h; PHE-10: 2063±128, PHE-5: 2055±104, C: 2055±547), however, PHE-10 tended to increase GLP-1 compared with PHE-5 (P=0.07) and C (P=0.08) (AUC, pmol/L*min; PHE-10: 2899±248, PHE-5: 2489±181, C: 2542±178). Our data suggest that the modest lowering of postprandial blood glucose by PHE is not mediated by slowing of gastric emptying, but via stimulation of insulin, probably by a direct effect of PHE on the pancreas, while the role of GLP-1 is unclear.

10:45 **Insulin Resistance Is Related To Olfactory Sensitivity For Food Odors Independent Of Bmi**

MARIA POESSEL[1,2,3], ANNETTE HORSTMANN[1,2,3,4]
[1]IFB AdiposityDiseases, University Medical Center, 04103 Leipzig, Germany, [2]Department of Neurology, Max Planck Institute for Human Cognitive and Brain Sciences, 04103 Leipzig, Germany, [3]Leipzig University Medical Center, CRC 1052A5 'Obesity Mechanisms', 04103 Leipzig, Germany, [4]Department of Psychology and Logopedics, Faculty of Medicine, University of Helsinki, 00290 Helsinki, Finland

Intro: The worldwide obese epidemic is a major health problem that is driven by the modern food environment. In recent years, it has been shown that smell perception plays a key role in unconscious decisions for foods and is therefore closely related to eating behavior. Since smell perception seems to be altered in obesity, this fact might crucially contribute to a poor diet leading to weight gain. However, the underlying mechanisms of impaired olfactory perception and altered hedonic response to food odors in obesity are not well understood yet. Since the olfactory system is closely linked to the endocrine system, we hypothesized that hormonal shifts that are associated with obesity might explain this relationship. **Methods:** In a within-subject repeated-measures design, we investigated sensitivity to a food and non-food odor in the hungry and sated state in 75 young healthy (26 lean, 25 overweight, 24 obese) participants (37 women). To determine metabolic health status and hormonal reactivity in response to food intake, we assessed pre- and postprandial levels of insulin, leptin, glucose and ghrelin. **Results:** Odor sensitivity did not depend on body weight status/BMI or metabolic state (hungry vs. sated). Interestingly, we could show a strong mediating effect of baseline insulin resistance on the relationship between BMI and olfactory sensitivity for the food odor only in the sated condition. In further applied regression models, we revealed that insulin resistance rather than obesity predicts low olfactory sensitivity for food odors in the sated state. **Conclusion:**Odor sensitivity in healthy individuals is not predicted by body weight status or BMI, but by metabolic health. Insulin resistance in particular is associated with a lower olfactory sensitivity after a meal.

11:00 **(Nita Award Winner) Intragastric Administration Of The Bitter Tastant, Quinine, Attenuates The Glycaemic Response To A Nutrient Drink In Healthy Lean Men**

VIDA BITARAFAN[1], PENELOPE CE FITZGERALD[1], TANYA J LITTLE[1], WOLFGANG MEYERHOF [2], TONGZHI WU[1], MICHAEL HOROWITZ[1], CHRISTINE FEINLE-BISSET[1]
[1]Adelaide Medical School, University of Adelaide, Adelaide, Australia, [2]Center for Integrative Physiology and Molecular Medicine, Saarland University, Homburg, Germany

The rate of gastric emptying and the release of gastrointestinal (GI) and pancreatic hormones are major determinants of postprandial blood glucose concentrations. Preclinical studies suggest that activation of GI bitter taste receptors potently stimulates the release of glucoregulatory GI hormones, including glucagon-like peptide-1 (GLP-1); however, data in humans are limited and inconsistent. We have evaluated the acute effects of intragastric administration (to avoid the unpleasant taste) of quinine on the glycaemic response to, and gastric emptying of, a mixed-nutrient drink. 12 healthy, lean men (age 25±5 years; BMI 23.3±1.4 kg/m^2) received on 3 separate occasions, in double-blind, randomised fashion, an intragastric bolus of 275 mg (Q275) or 600 mg (Q600) quinine-hydrochloride, or control (C), 30 min before a mixed-nutrient drink (500 kcal, 74 g

carbohydrate). Plasma glucose, GLP-1 and insulin concentrations were measured at baseline and for 30 min after quinine alone, and for 2 h following the drink (t = 0-120 min). Gastric emptying of the drink was measured for 2 h by ^{13}C-acetate breath test. Q600 alone slightly increased both plasma GLP-1 and insulin, and Q275 increased insulin (all P< 0.05). In response to the drink, Q600, but not Q275, reduced plasma glucose compared with C (peak (mmol/L); Q600: 5.7±0.2, Q275: 6.3±0.3, C: 6.8±0.4; P< 0.05). Moreover, Q600 increased insulin at t = 30 min, and both Q275 and Q600 increased GLP-1 at t = 45 and 60 min (all P< 0.05). Quinine did not affect gastric emptying. In conclusion, intragastric quinine reduces postprandial blood glucose, at least in part, by stimulating GLP-1 and insulin secretion, but not via slowing of gastric emptying.

11:15 **Preview - Lifestyle Intervention For Prevention Of Type-2 Diabetes In > 2,200 Adults: Results From A 3-Year Multinational Randomised Trial Comparing 2 Diets And 2 Exercise Strategies**

MARGRIET S. WESTERTERP-PLANTENGA[1], MATHIJS DRUMMEN[1], TANJA C.M. ADAM[1], MIKAEL FOGELHOLM[2], IAN MACDONALD[3], J. ALFREDO MARTINEZ[4], TEODORA HANDJIEVA-DARLENSKA[5], GARETH STRATTON[6], MAIJA HUTTUNEN-LENZ[7], TONY LAM[8], JOUKO SUNDVALL[9], SALLY POPPIT[10], JENNIE BRAND-MILLER[11], THOMAS M. LARSEN[12], PIA CHRISTENSEN[12], ANNE RABEN[12]

[1]Maastricht University, Maastricht, Netherlands, [2]University of Helsinki, Helsinki, Finland, [3]University of Nottingham, Nottingham, United Kingdom, [4]University of Navarra, Pamplona, Spain, [5]University of Sofia, Sofia, Bulgaria, [6]University of Swansea, Swansea, United Kingdom, [7]University of Stuttgart, Stuttgart, Germany, [8]NetUnion, Lausanne, Switzerland, [9]National Institute for Health and Welfare, Helsinki, Finland, [10]University of Auckland, Auckland, New Zealand, [11]University of Sydney, Sydney, Australia, [12]University of Copenhagen, Copenhagen, Denmark

The PREVIEW lifestyle intervention study (www.previewstudy.com), to date the largest of its kind hypothesized that a high-protein (HP), low-glycaemic index (GI) diet is superior to a moderate-protein (MP), higher-GI diet, and that high-intensity (HI) physical activity (PA) is superior to medium intensity (MI) PA, for prevention of type-2 diabetes (T2D). A 3 year randomized trial with 4 arms was conducted in 8 centers (DK, FI, NL, UK, ES, BG, AU, NZ). A total of 2,223 adults with prediabetes (25-70y, BMI≥25 kg/m2) started and 962 completed the study. Those with body weight loss of ≥ 8% after 2-month weight reduction using a low-energy diet started a 34-month weight maintenance phase on 1 of 4 treatments: HP-HI, HP-MI, MP-HI, and MP-HI. The primary endpoint was incidence of T2D over 3 years. Sub-studies assessed associations of changes in insulin sensitivity (IS) with changes in food-reward related brain signaling, metabolic flexibility (MF) assessed in the respiration chamber, and MRI/MRS assessed intrahepatic triglycerides (IHTG). After 3 years 62 T2D cases were observed, with no difference between the diets (Hazard ratio, HR, MP to HP:1.22(0.73–2.05, p=0.45) or the 2 PA regimes (HR, HI vs MI:1.35, p=0.27). Body weight change was -10.8kg (-11.9 kg to -9.7 kg), or 11%, remaining at -4.7 kg (-6.4 kg to –3.0 kg) at 3 y; HOMA-IR changed from 3.8±0.8 to 2.7±0.8. Protein intake and changes in IS were inversely related to changes in food reward related brain signaling, and to IHTG. IS was positively related to MF. In conclusion, a HP-low GI diet and HI PA were not superior for prevention of T2D. Reduced insulin resistance was linked with decreased IHTG, increased metabolic flexibility, and food intake control supported by decreased food reward related brain signaling.

11:30 **The Identification And Characterisation Of Glucose-Dependent Insulinotropic Polypeptide Receptor-Expressing Cells In The Hypothalamus**

ALICE E ADRIAENSSENS, EMMA K BIGGS, TAMANA DARWISH, TANMAY SUKTHANKAR, MILIND GIRISH, JOSEPH POLEX-WOLF, BRIAN Y LAM, ILONA ZVETKOVA, GILES SH YEO, CLEMENCE BLOUET, FIONA M GRIBBLE, FRANK REIMANN

1Institute of Metabolic Science & MRC Metabolic Diseases Unit, University of Cambridge, Cambridge, United Kingdom

Ambiguity regarding the role of glucose-dependent insulinotropic polypeptide (GIP) in obesity arises from conflicting reports asserting that both GIP receptor (GIPR) agonism and antagonism are effective strategies for inhibiting weight gain. We sought to characterise GIP-responsive cells in the brain and investigated how activation of hypothalamic GIPR cells affects food intake. To enable identification, purification, and manipulation of GIPR-expressing cells we created GIPR-Cre knock-in mice. Single-cell RNA sequencing (scRNAseq) of purified hypothalamic *Gipr* cells was used in combination with real time calcium imaging in primary cultures to probe the functional importance of key genes expressed in *Gipr* neurons. The effects of acute modulation of hypothalamic *Gipr* cell activity on food intake was assessed after selective AAV mediated expression of Cre-dependent designer receptors exclusively activated by designer drugs (DREADDs). Staining for a fluorescent reporter expressed under the control of the *Gipr* promoter revealed that GIPR is present in the arcuate and dorsomedial nuclei of the hypothalamus. scRNAseq analysis identified sub-populations of hypothalamic *Gipr* cells, including clusters exhibiting transcriptomic signatures for oligodendrocytes and neurons, with the latter expressing high levels of somatostatin, but little proopiomelanocortin or agouti-related peptide. A subset of neurons exhibited calcium responses to cholecystokinin. Activation of G_q DREADDS in hypothalamic *Gipr* cells supressed food intake *in vivo*. *Gipr* is expressed in key feeding centres of the hypothalamus. The anorectic tone exerted upon acute stimulation of these cells potentially indicates GIPR positive neurons underlie recent reports of appetite suppression following GIPR/GLP1R dual agonism.

11:45 **Effects Of Intranasal Insulin On Brain Connectivity And Cognition In Overweight/Obese Adolescents**

TUKI N ATTUQUAYEFIO[1], IRIS HOVENS[1], ALEX DIFELICEANTONIO[1], MICHAEL FARRUGIA[1],

KATHRYN WALL[1], NICOLA SANTORO[2], SONIA CAPRIO[2], DANA SMALL[1]

[1]Department of Psychiatry, Yale University, New Haven, CT, United States, [2]Department of Pediatrics, Yale University, New Haven, CT, United States

Objectives: The overarching goal of this project is to determine the relative contribution of adiposity, peripheral glucose intolerance and central insulin resistance on neurocognition in obese youth. Here we report preliminary findings from an ongoing study examining the influence of intranasal insulin administration on resting state brain connectivity and cognition. **Methods:** Eleven youth aged 8-18, recruited from the Pathogenesis of Youth Onset Diabetes (PYOD) longitudinal study, underwent resting state fMRI scans followed by cognitive assessment after placebo and after intranasal insulin administration on two separate days. Whole brain connectivity was estimated from 3 ROIs: midbrain, hippocampus and dorsolateral prefrontal cortex. Cognitive measures included delayed non-matching to sample and spatial working memory tasks. **Results:** Preliminary analyses identified a negative association between BMI on both cognitive tasks following placebo that was eliminated upon intranasal insulin administration. Examination of rsfMRI revealed increased connectivity between left and right dorsolateral prefrontal cortex following intranasal insulin. No other ROIs showed changes in connectivity, nor did we observe significant improvements in cognitive performance related to these ROIs following insulin administration. **Conclusion:** Preliminary analyses from our ongoing study suggest that intranasal insulin influences cognitive and brain function in overweight and obese youth. Data collection and analyses are ongoing with in-depth phenotyping including a full neuropsychological battery, hyperinsulinemic-euglycemic clamp, oral glucose tolerance test and abdominal and liver fat measured with MRI.

12:00 **Insulin Signaling In Agrp Neurons Coordinates Glucose Metabolism With Feeding**

GARRON T DODD[1], ROBERT S LEE[2], JENS C BRUNING[3], TONY TIGANIS[2]

[1]Department of Physiology, The University of Melbourne , Melbourne, Australia, [2]Monash Biomedicine Discovery Institute, Melbourne, Australia, [3]Department of Neuronal Control of Metabolism, Max Plank Institute for Metabolism Research, Cologne, , Germany

Insulin regulates glucose metabolism by eliciting effects on peripheral tissues as well as the brain. Insulin receptor (IR) signalling inhibits AgRP-expressing neurons in the hypothalamus to contribute to the suppression of hepatic glucose production (HGP), whilst AgRP neuronal activation attenuates brown adipose tissue (BAT) glucose uptake. Whilst this suggests a link between postprandial signalling and the neuronal control of glucose metabolism the precise neuronal mechanism mediating this response remain unclear. Recent evidence suggests that insulin signalling in neurons is mediated by the insulin receptor phosphatase, TCPTP. The expression of TCPTP in AgRP neurons is elevated during fasting where it acts to suppresses IR signalling and is degraded after feeding to promote IR signalling. TCPTP acts as a molecular switch coordinating AgRP insulin signalling with nutritional status. In this study, we used transgenic mouse models to assess the influence of modulating TCPTP in AgRP neurons in the control of glucose metabolism. We found that TCPTP deletion in AgRP neurons hypersensitised AgRP neurons to insulin, resulting in enhanced whole-body insulin sensitivity, reduced HGP and increased glucose uptake in BAT and browned white adipose tissue. TCPTP deficiency in AgRP neurons promoted the intracerebroventricular insulin-induced repression of HGP in otherwise unresponsive food-restricted mice. Interesting, the effect on HGP was lost in fed mice where hypothalamic TCPTP levels are reduced, causally linking the effects on glucose metabolism with the IR signalling in AgRP neurons. These findings demonstrate that TCPTP controls IR signalling in AgRP neurons to coordinate whole-body glucose metabolism with feeding.

12:15 **Exendin-4 Conjugated To Vitamin B12 Improves Glucose Tolerance In Shrews And Lean Type 2 Diabetic Rats Without Inducing Vomiting Or Hypophagia**

TITO BORNER[1], IAN C. TINSLEY[2], EVAN D. SHAULSON[1], LAUREN M. STEIN[3], JAYME L. WORKINGER[2], ROBERT P. DOYLE[2,4], MATTHEW R. HAYES[3], BART C. DE JONGHE[1]

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

Glucagon-like peptide-1 receptor (GLP-1R) agonists used to treat type 2 diabetes mellitus (T2DM) often produce nausea, vomiting (emesis), and in some patients, undesired anorexia. Notably, these side effects are caused by direct central GLP-1R activation. Our group developed a conjugate of vitamin B12 bound to the GLP-1R agonist exendin-4 (Ex4), which shows reduced hindbrain penetrance. Here, we evaluated the efficacy of the B12-Ex4 conjugate to improve glucose tolerance without inducing anorexia in Goto Kakizaki (GK) rats, a lean T2DM model. Since rodents are a non-vomiting species, we also utilized the musk shrew (*Suncus murinus*), a mammalian model capable of emesis, to test B12-Ex4 on glycemic profile, feeding and vomiting. In both species, native Ex4 and B12-Ex4 equivalently blunted the rise in blood glucose levels following glucose administration during a glucose tolerance test. Remarkably, while Ex4 led to the expected stress-mediated hyperglycemia in GK rats prior to glucose delivery, no change in blood glucose was observed after B12-Ex4 administration. In both GK rats and shrews, acute administration of native Ex4 significantly suppressed 24h food intake leading to body weight loss; in contrast equimolar administration of B12-Ex4 had no effect on feeding and body weight. Importantly, the number of shrews experiencing emesis after systemic B12-Ex4 was greatly diminished compared to native Ex4. However, when administered centrally, both induced profound emesis; functionally validating the reduced hindbrain permeability of B12-Ex4. Collectively, these findings

highlight the potential therapeutic value of B12-Ex4 as a novel treatment for T2DM, especially in a non-obese population, with drastically reduced adverse effects but similar glucoregulation to native Ex4.

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

12:45 - 1:45 PM	Mission 1
Meet the Scientist Professional Development Panel	

During this career development panel and lunch, our panel of scientists will share their advice for pursuing careers within and outside of academia. Panelists will answer questions from the audience and share their expertise across topics such as: transferrable skills for alt-academia careers, navigating the academic job market, early-career grant writing, and finding work-life balance. A box lunch will be available to the first 50 attendees.

2:00 - 4:00 PM	Progress
SYMPOSIUM 3: Lateral Hypothalamus and Ingestive Behavior	

Chair(s): Susanne la Fleur and Emily Noble

2:00 **Circuit And Signals Of The Lateral Hypothalamus: Inputs-Processing-Outputs**

DENIS BURDAKOV
ETH Zurich, Zurich, Switzerland

We have been working on linking historic observations relating to the lateral hypothalamus (LH) – such as glucose-sensing and control of cognition and action - to specific genetically-defined LH cells, circuits, and signals. Patch-clamp recordings from genetically-defined LH neurons revealed that nutrient signals such as glucose and amino-acids alter LH activity in a cell-type-specific way. LH neuron such as orexin neurons co-release peptides and fast-transmitters, and our optogenetic and electrophysiological data indicate that they are released at different firing rates, and implement different downstream computations in wider LH circuits. Monosynaptic retrograde circuit tracing revealed that LH cells that sense nutrient signals also receive brain-wide direct inputs. Optogenetics-assisted circuit mapping, and opto and chemogenetic interference during behaviour, delienated functional LH microcircuits, and large-scale long-range LH circuits, that convert cell-type-specific LH signals into specific aspects of cognition and action. In turn, cell-type-specific, real-time LH recordings during behaviour indicated that LH activity changes rapidly and cell-type-specifically during interactions with the external environment, indicating a role of moment-to-moment LH dynamics in rapid sensorimotor control.

2:30 **Comfort For The Troubled Mind: Unravelling The Neural Basis For Stress-Feeding**

LOUISA E. LINDERS[1], LEFKOTHEA PATRIKIOU[1], MARIANO SOIZA-REILLY[2], ROGER A.H. ADAN[1], FRANK J. MEYE[1]
[1]Dept Translational Neuroscience, Brain Center, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands, [2]IFIBYNE, University of Buenos Aires, Buenos Aires, Argentina

Stressful events can form a potent trigger to overconsume palatable high-caloric food. This represents a core problem in obesity and several eating disorders. The exact neural circuit adaptations governing this behavior remain limitedly understood. The mesolimbic dopamine system plays a crucial role in the motivation to obtain (food) rewards and is also sensitive to stressors, making this an important candidate system to mediate the effects of stress on reward seeking. In the current study we set out to investigate how exposure to stress alters specific synaptic inputs to the mouse ventral tegmental area (VTA), a key node of the reward system. Activity in the VTA is controlled by a variety of synaptic inputs of different origins. We addressed which of these are sensitive to stress-induced modifications, by employing a strategy combining optogenetics and slice electrophysiology to assess stress-driven plasticity of specific VTA inputs. We stereotactically injected viral vectors to express channelrhodopsin into nuclei that innervate the VTA. After 3-4 weeks, mice were exposed to periods of stress, after which whole-cell voltage clamp recordings were made in the VTA and input-specific synaptic responses were evoked by short light pulses. Our findings suggest that stress indeed alters the synaptic strength of inputs to the VTA. Currently we are assessing the relevance of different types of afferents in this process, and aim to determine the behavioral relevance of their altered strength in terms of food consumption.

3:00 **Hypothalamic Cell Types And Circuits That Drive Survival Behaviors**

YEKA APONTE [2]
[1]NIH , Baltimore, MD, United States, [2]Johns Hopkins , Baltimore, MD, United States

Across species, motivated states such as food-seeking and consumption are essential for survival. The lateral hypothalamys (LH) is known to play a fundamental role in regulating feeding and reward-related behaviors. However, the contributions of neuronal subpopulations in the LH have not been thoroughly identified. Here we examine how lateral hypothalamic leptin receptor-expressing (LHlepr) neurons, a subset of GABAergic cells, regulate motivation in mice. We find that LHlepr neuronal activation significantly increases progressive ration

(PR) performance, while inhibition decreases responding. Moreover, we mapped LHlepr axonal projections and demonstrated that they target the ventral tegmental area (VTA), form functional inhibitory synapses with non-dopaminergic VTA neurons, and their activation promotes motivation for food reward. Finally, we find that LHlepr neurons also regulate motivation to obtain water, suggesting that they may play a generalized role in motivation. Together, these results identify LHlepr neurons as modulators within a hypothalamic-ventral tegmental circuit that gates motivation.

3:30 **Central Neurotensin Orchestrates Drinking And Feeding Behavior**

GINA M LEINNINGER
Michigan State University, East Lansing, MI, United States

It has long been recognized that the lateral hypothalamic area (LHA) of the brain is necessary for coordinating ingestive behavior. Yet, it remains unclear how the neurochemically-distinct neural populations within the LHA specifically coordinate drinking vs. feeding. Pharmacological data suggested that the neuropeptide neurotensin (Nts) has anorectic and prodipsic effects, and hence might differentially direct ingestive behaviors. Since Nts is expressed within the LHA, we hypothesized that "LHA Nts neurons" might coordinate specific ingestive behaviors compared to other known LHA populations, but the lack of reliable methods to detect Nts soma limited further study. To overcome this limitation, we used genetic tools to visualize Nts neurons *in vivo*, which revealed that LHA Nts neurons are numerous and neurochemically distinct from other LHA neurons that promote both intake behaviors. Furthermore, activation of LHA Nts neurons promotes voracious water intake and locomotor activity while restraining feeding, suggesting that these neurons differentially orchestrate ingestive behaviors. This talk will discuss the circuits, neuropeptide signaling mechanisms and behaviors by which LHA Nts neurons coordinate the need for food and water with intake behavior, and will assess whether this novel LHA neuronal population might be a rational pharmacological target to treat disease-disrupted energy or water balance.

2:00 - 4:00 PM	Mission 1
ORAL SESSION 4: Maladaptive Eating	

Chair(s): Kellie Tamashiro and Menna Price

2:00 **Prefrontal Cortex Activation Predicts Food-Specific Impulsive Behavior After An Impulsivity-Focused Treatment In Patients With Binge Eating Disorder**

STEPHANIE KULLMANN[1], KATHRIN SCHAG[2], RALF VEIT[1], MAIKE BORUTTA[1], STEPHAN ZIPFEL[2], KATRIN GIEL[2], HUBERT PREISSL[1]

[1]Institute for Diabetes Research and Metabolic Diseases of the Helmholtz Center Munich at the University of Tübingen German Center for Diabetes Research (DZD e.V.), Tübingen, Germany, [2]Department of Psychosomatic Medicine and Psychotherapy, University Hospital Tübingen, Tübingen, Germany

Behavioral and cognitive control are vital for healthy eating behavior. Patients with binge eating disorder (BED) suffer under recurrent binge eating episodes accompanied by subjective loss of control. In the current study, we investigated the frontal network using functional near-infrared spectroscopy (fNIRS) during a food specific go/no-go task to assess cognitive control (i.e. response inhibition) in 25 patients with BED (BMI range 22.6-59.7 kg/m^2). Patients with BED were invited to undergo fNIRS measurements before treatment, directly after treatment and 3 months afterwards. As this was part of a randomized controlled trial, patients with BED were either randomized to the treatment group or a control group. The treatment group (n=11) received 8 weekly sessions of an impulsivity-focused group intervention, the control group (n=14) received no treatment. As previously reported, we found a significant response inhibition effect, resulting in increased oxygenated hemoglobin response in prefrontal cortex. BED patients with higher trait impulsivity showed a weaker activation of the dorsolateral prefrontal cortex during response inhibition, predominantly in the right hemisphere. Interestingly, three months after the therapy, patients of the treatment group increased their right dorsolateral prefrontal cortex during response inhibition. Likewise, improved prefrontal cortex activation predicted decreased impulsivity and eating disorder pathology after treatment. Our results suggest that patients with BED have limited resources to activate the dorsolateral prefrontal cortex when asked to inhibit a certain behavior. However, behavioral therapy targeting impulsive eating behavior can improve dorsolateral prefrontal cortex recruitment during response inhibition.

2:15 **Weight Suppression, Resting Energy Expenditure And Related Hormones In Bulimia Nervosa**

MICHAEL LOWE[1], NICOLE VIRZI[1], KIRSTIE HERB[1], RACHEL KORN[2], LAUREL MAYER[2]

[1]Drexel University , Philadelphia, PA, United States, [2]Columbia University, New York City, NY, United States

Weight suppression (WS) refers to the difference between highest past weight at adult height and current weight. Substantial evidence indicates that WS is a prospective predictor of future weight gain and numerous other characteristics in eating disordered individuals. The extent to which biological consequences of WS account for its predictive utility is largely unexamined. We studied the relation between WS and both resting energy expenditure (REE) and related hormones in BN. Eighty-nine women with full or partial DSM5-defined bulimia nervosa were recruited. After an overnight fast, REE was measured by indirect calorimetry (normalized for DXA-assessed lean tissue) and blood samples were drawn for leptin, ghrelin, thyroid function, insulin and glucose. Linear regressions were used to conduct analyses. On average, participants had been ill for 9.2 ± 6.5 years, were 25.3 ± 5.6 years old, BMI of 23.6 ± 4.0 kg/m^2 and WS of 7.97 $\pm$ 8.08 kg. Level of WS ranged from 0-43.5kg. Controlling for relevant variables, WS was not related to REE, but was inversely related to leptin ($p < .05$), T3 ($p < .05$), insulin ($p < .001$) and glucose ($p < .02$), suggestive of a regulatory response to WS. Given the REE findings, the hormonal results may reflect stronger appetitive drive, rather than greater metabolic efficiency, in weight-suppressed individuals. WS is related to some but not all expected weight loss-related metabolic alterations. These changes may mediate the relationship between WS, future weight gain and behavioral features of the illness.

2:30 **Gdf15 Acts Through A Subset Of Brainstem Gfral/Cck Neurons To Induce Anorexia**

AMY A WORTH[1], ROSIE SHOOP[1], KATIE TYE[1], CLAIRE H FEETHAM[1], EMILY BEEBE[2], JAMES DUNBAR[2], TAMER COSKUN[2], PAUL EMMERSON[2], SIMON M LUCKMAN[1]

[1]University of Manchester, Manchester, , United Kingdom, [2]2Lilly Research Laboratories, Eli Lilly & Company, Indianapolis, IN, United States

The cytokine, GDF15, is produced by a number of tissues in pathological states which cause cellular stress, including cancer, cardiac failure and obesity. Although a full understanding of its role in disease progression is unclear, the fact that it can cause dramatic weight reduction when over expressed, suggests a potential role in disease-related anorexia rather than normal homeostasis. The GDF15 receptor, GFRAL, was described simultaneously by four pharmaceutical companies in 2017, and found to be located only in the brainstem medulla oblongata (Mullican *et al*., 2017, *Nat Med* 23, 1150; Yang *et al*., 2017, *Nat Med* 23, 1158; Emmerson *et al*., 2017, *Nat Med* 23, 1215; Hsu *et al*., 2017, *Nature* 550, 255). Here we demonstrate that GFRAL is contained in a subset of cholecystokinin neurons which span the area postrema and the dorsal nucleus of the tractus solitarius. $GFRAL^{AP/NTS}$ neurons are activated by GDF15, but not satiety signals or the nausea-inducing agent, LiCl. GDF15 supports conditioned taste and place aversions, while the anorexia it causes can be blocked by a

monoclonal antibody directed at GFRAL or by disrupting CCK signalling. The anorectic downstream pathways include neurons in the parabrachial and paraventricular nuclei, the central amygdala and oval bed nucleus of the stria terminalis. The cancer therapeutic drug, cisplatin, induces the release of GDF15 and activates $GFRAL^{AP/NTS}$ neurons, as well as causing significant reductions in food intake and body weight. These metabolic effects of cisplatin are completely abolished by treatment with the GFRAL monoclonal antibody. Our results suggest that GFRAL neutralising antibodies or GFRAL antagonists may provide a possible co-treatment opportunity for patients undergoing chemotherapy.

2:45 **Examination Of Orofacial Response To Good And Bad Tastants Across A Time Course Of The Activity-Based Anorexia Model In Adolescent Female Rats.**

MATTHEW M. HURLEY, VICTORIA X. CHEN, ASHRAF N. NAWARI, S. ANDREW ASTON, LUCAS J. WILES, ETHAN J. GOODMAN, SEVA G. KHAMBADKONE, KELLIE L. TAMASHIRO, TIMOTHY H. MORAN
Johns Hopkins University School of Medicine, Baltimore, MD, United States

Rats in the activity-based anorexia (ABA) rodent model of anorexia nervosa exhibit by excessive wheel running, rapid weight loss (25%) and limited food intake. Previously our lab has shown that adolescent female rats subjected to ABA develop a conditioned taste aversion faster than controls suggesting that the ABA exposure may change the hedonic value of tastants. To test this hypothesis, we evaluated taste reactivity and analyzed orofacial responses to tastants delivered involuntarily into the rodent's oral cavity. This method of tastant delivery produces evolutionarily conserved (human infant, monkey, rodent) orofacial responses that are considered appetitive ('liking') responses or aversive ('disliking') responses. We assessed cumulative 'liking'/'disliking' responses in six 1-minute tastant trials (water, 0.01M, 0.1M, 1.0M sucrose, 0.0003M, 0.003M quinine) prior to ABA (baseline) and after 10 days weight recovery from ABA. Data were analyzed by ANOVA (repeated measures as appropriate) or paired t-test. We found that animals with a history of ABA displayed significantly fewer appetitive responses to 1.0M sucrose (*paired t-test*; p=0.004) compared to their baseline values. This phenomenon was not observed in the running wheel (unlocked wheel for the same duration as the ABA group with ad lib food) or sedentary (locked wheel/ad lib food) control groups. Additionally, we examined the relationship between cumulative wheel running during the ABA paradigm and the degree to which appetitive response score was attenuated following ABA. We found a significant negative correlation between running activity and hedonic perception score. Taken together, our findings demonstrate that ABA experience negatively impacts perception of palatable tastants in weight-recovered female rats.

3:00 **Modeling Of Food Intake Among Restrained And Unrestrained Eaters: Implications For The Normative Theory Of Eating**

LENNY R VARTANIAN
UNSW Sydney, Sydney, Australia

Social models are thought to influence people's food intake by providing an upper limit for how much it is appropriate to eat. From this normative perspective, eating with a companion who eats a lot does not require one to eat more than one normally would. However, for individuals who tend to restrict their food intake (e.g., restrained eaters), eating with a companion who eats a lot might give them permission to overindulge. This study examined the effect of dietary restraint on modeling of food intake by combining data from five previously-published studies. Each of the studies included: a no-norm (eat alone) condition; a high-intake norm condition; and a low-intake norm condition. Across the five studies, there were a total of 253 unrestrained eaters and 190 restrained eaters. Overall, participants ate more in the high-intake norm conditions than in the no-norm conditions (d=0.47, p=.001). However, subgroup analyses indicated that the magnitude of the effect was larger for restrained eaters (d=0.66, p=.005) than for unrestrained eaters (d=0.35, p=.07). In contrast, when comparing the no-norm conditions to the low-intake norm conditions, there was no difference between restrained and unrestrained eaters in the magnitude of the modeling effect: both groups ate less when presented with the low-intake norm compared to no norm (d=-0.43, p< .001). These findings provide support for the normative theory of eating which suggests that other people's food intake provides an upper limit for appropriate intake. Low-intake norms consistently result in reduced food intake. High-intake norms do not require one to overeat but, by providing a high ceiling for appropriate intake, can lead to "disinhibition" among individuals who tend to restrict their food intake.

3:15 **Impulsivity Influences Energy-Dense Food Consumption In Women With Generalized Anxiety Disorder**

ROBERTA DALLE MOLLE[1,2], NATASHA K.O. FONSECA[3], MARIANNA A. COSTA[4], FRANCINE G. GONÇALVES[4], ALICE C. SILVA[5], YLANA RODRIGUES[5], PATRICIA P. SILVEIRA[6], GISELE G. MANFRO[3,4]
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Many factors can influence eating behavior of anxious individuals, however the factors that make some anxious

patients overeat or adopt a restrained approach to eating still need to be elucidated. Our aim was to investigate the association between impulsivity, self-compassion, and energy-dense food consumption in women with Generalized Anxiety Disorder (GAD). Fifty-one adult females patients with GAD had anthropometric data assessed and answered the Self-Compassion Scale, the Food Frequency Questionnaire, and the Barratt Impulsiveness Scale (BIS-11). Pearson correlation and multiple linear regressions were performed. All regression models were adjusted by age and body mass index (BMI). In GAD female patients (mean age= 33 ± 11.32 years; mean BMI= 27.3 ± 6.35), impulsivity was positively correlated to the intake of total fat (r= 0.35, p= 0.015), saturated fat (r= 0.37, p= 0.008) and sugar (r= 0.42, p= 0.003). Self-compassion was negatively correlated to the consumption of total fat (r= -0.29, p= 0.046) and saturated fat (r= -0.29, p= 0.043). In the regression analyses, impulsivity predicts total fat intake (B= 1.51, Beta= 0.314, P= 0.029; Model adjusted R^2= 0.138; p= 0.032), saturated fat intake (B= 0.655, Beta= 0.362, P= 0.012; Model adjusted R^2= 0.139; p= 0.031) and sugar intake (B= 2.929, Beta= 0.349, P= 0.014; Model adjusted R^2= 0.175; p= 0.014). We showed that impulsivity was a prominent factor, among those analyzed, in predicting the consumption of fats and sugar in female patients diagnosed with GAD. Our findings could contribute to improve the knowledge of the eating behavior in this population that is vulnerable to eating disorders and obesity.

3:30 **Prefrontal Circuit Activity Influences Susceptibility To Activity-Based Anorexia In Rats**

CLAIRE J FOLDI, LAURA K MILTON, BRIAN J OLDFIELD
Monash University, Biomedicine Discovery Institute, Melbourne, Australia

Anorexia nervosa (AN) has the highest mortality rate of any psychiatric disease, yet available treatments are largely ineffective, in part due to a lack of insight into the neurobiological drivers that underpin the condition. Functional neuroimaging in AN patients suggests that overactive cognitive neurocircuitry contributes to pathological body weight loss. Using pathway specific chemogenetics in conjunction with the activity-based anorexia (ABA) rat model, we hypothesized that decreasing activity in neurons of the medial prefrontal cortex (PFC) with direct projections to ventral reward circuits would improve body weight maintenance in ABA. Female Sprague-Dawley rats (*n*=33; 6 wks old) underwent bilateral stereotaxic injections of retrogradely-transporting Cre (AAV-pmSyn1-EBFP-Cre) into the nucleus accumbens (NAc) and coincident injections of either inhibiting (AAV-hSyn-DIO-hM4D(Gi)-mCherry), activating (AAV-hSyn-DIO-hM3D(Gq)-mCherry) or control (AAV-hSyn-DIO-mCherry) DREADD viruses into the PFC. During exposure to the ABA paradigm, which involves unhindered access to a running wheel and time-limited (90 min) access to food, all rats were administered clozapine-n-oxide (CNO) daily (0.3-3 mg/kg i.p.) at the onset of the dark phase. Chemogenetic inhibition of PFC-NAc projection neurons decreased susceptibility to body weight loss during ABA (χ^2=8.77, *p*=0.013) by increasing food anticipatory activity (FAA; *p*=0.011) and subsequent food intake (*F*=4.14, *p*=0.025). Conversely, activation of this pathway exacerbated hyperactivity induced by food restriction (*F*=6.06, *p*=0.006). Our data indicate that prefrontal circuits impact on food intake and running activity, both essential elements of the ABA phenotype and the AN condition that contribute to pathological body weight loss.

3:45 **Manipulation Of Melanocortin 3 Receptor Potently Regulates Feeding And Anxiety**

PATRICK R SWEENEY[1], MICHELLE BEDENBAUGH[2], PAOLO GRIECO[3], RICHARD B SIMERLY[2], ROGER D CONE[1]
[1]University of Michigan, Ann Arbor, MI, United States, [2]Vanderbilt University, Nashville, TN, United States, [3]University of Naples Federico II, Naples, Italy

Disorders of negative energy balance, such as anorexia nervosa and disease cachexia, are characterized by decreased food intake, dangerously low BMI, and an increased risk of anxiety and depression. Despite the severe consequences of these disorders, few pharmacological strategies exist to stimulate feeding and reduce anxiety in these at-risk patient populations. Here, we report that newly characterized MC3R agonists potently stimulate feeding, increase body weight, and reduce anxiety in an AgRP neuron dependent manner. Consistently, we identify that the MC3R exhibits significantly higher expression in AgRP neurons than anorexigenic POMC neurons. Chemogenetic activation of all arcuate neurons expressing MC3R phenocopies MC3R agonist treatment, both stimulating feeding and body weight and reducing anxiety-related behavior. Conversely, chemogenetic inhibition of these cells reduces feeding and increases anxiety-related behavior. Finally, we demonstrate that mice lacking the MC3R display multiple behavioral phenotypes resembling anorexia nervosa, such as enhanced anxiety behavior and increased susceptibility to multiple forms of stress-induced anorexia. Taken together, these results suggest that stimulation of the MC3R is a promising therapeutic approach for combating disorders at the intersection of energy metabolism and emotion, such as anorexia nervosa.

4:00 - 4:30 PM	Transit Zone
Coffee Break	

4:30 - 6:30 PM	Progress
SYMPOSIUM 4: Presidential Symposium: Insulin and Eating Disorders	

Chair(s): Ruth Harris

4:30 **Eating Behaviors In Adolescents At Risk For Type 2 Diabetes**

JACK A. YANOVSKI
National Institutes of Health, Bethesda, MD, United States

Pediatric studies examining risk for type 2 diabetes (T2D) indicate there is significant heritability of this condition, but that the environment also plays an important role. Behaviors, including eating behaviors relevant for T2D development, can be affected by genetic, epigenetic, and environmental factors. This presentation will discuss the disinhibited eating behaviors commonly observed in children at-risk for type 2 diabetes. Disinhibited eating refers to a lack of self-regulation over food consumption, including behaviors such as eating in the absence of hunger (EAH) and loss-of-control-eating (LOC-eating). EAH is the intake of palatable food in the absence of physiological hunger, in response to emotional and/or external cues such as the availability of highly palatable food. Another form of disinhibited eating is LOC-eating, referring to perceived overeating accompanied by a subjective sense of not being able to control what or how much one is eating. Both EAH and LOC eating are commonly observed in children and adolescents with overweight and obesity and their prevalence is high in children at-risk for type 2 diabetes. Youth who report LOC are more likely to gain excess weight and body fat over time and to show a worsening in components of metabolic health that elevate T2D risk. In-lab data suggest children with LOC have greater intake of palatable foodstuffs that may be mechanistically linked to metabolic dysfunction. Some data further suggest children with LOC may demonstrate greater leptin resistance as well as evidence for greater inflammation versus those without LOC. It remains to be shown if Interventions directed at reducing disinhibited eating behaviors in children and adolescents are effective preventive strategies for T2D.

5:00 **Brain Insulin Action And Its Effect On Food-Related Behavior**

HUBERT PREISSL[1,2]
[1]Institute for Diabetes Resaerch and metabolic diseases of the Helmholtz Center Munich at the University of Tübingen, Tübingen, Germany, [2]Geman Center for Diabetes Research (DZD e.V.), Tübingen, Germany

Insulin is a major postprandial hormone and its peripheral action is an important contributor to metabolic health and diseases. Over the last years, we were able to show that specifically insulin action in the brain has a plethora of effects. Brain insulin action and especially brain insulin resistance characterize the obese state and predict success of life style interventions on the long run. In addition, brain insulin action is the main regulator of peripheral substrate distribution. Brain insulin action during early life is already affected by the metabolic state of the mother during pregnancy. In my presentation, I will give an overview of brain insulin action and how it affects eating behavior in normal and diseased state.

5:30 **Insulin And Eating Disorders**

JANET TREASURE
KCL, London, United Kingdom

Modelling clinical and epidemiological features of eating disorders into the neuroscience of appetite Innovative work on animal models has been highly informative in explaining the emergence of eating disorders in cohorts born after 1950. It has also led to the birth of the controversial concept of food addiction. The intermittent consumption of processed food/drinks with added sugar, fat and salt has been implicated as a key factor. Other clinical findings which need to be considered are the 2-3 fold increased risk of developing eating disorders in people with type 1 diabetes and individuals who purge . A common thread underpinning these high risk disorders is poor regulation of blood glucose due to insufficient or ineffective insulin. The rate of change of glucose has been hypothesised to set in motion neuroadaptive changes in dopamine processes that might underpin addictive behaviours. These conceptual models have real potential to inform the development of treatments for eating disorders. Treasure, J., Leslie, M., Chami, R., & Fernández-Aranda, F. (2018). Are trans diagnostic models of eating disorders fit for purpose? A consideration of the evidence for food addiction. *European Eating Disorders Review, 26*(2), 83-91. doi:10.1002/erv.2578 Wiss, D. A., & Brewerton, T. D. (2016). Incorporating food addiction into disordered eating: the disordered eating food addiction nutrition guide (DEFANG). *Eat Weight Disord*. doi:10.1007/s40519-016-0344-y

6:00 **Novel Islet Peptides And Hypoglycemia Unawareness: Targeting Glucagon Production**

GINA L. C. YOSTEN
Saint Louis University, Saint Louis, MO, United States

Hypoglycemia is a major complication of diabetes which when severe or recurrent can lead to confusion, seizures, coma, and death. Recurrent hypoglycemia or increased disease duration can lead to “hypoglycemia

unawareness," in which patients lose the ability to recognize the symptoms of hypoglycemia, leading to an increased risk of severe hypoglycemia and death. Hypoglycemia unawareness is accompanied by blunted hormonal responses to hypoglycemia. In particular, insufficient glucagon release appears to be the major factor contributing to the failed counterregulatory responses that characterize hypoglycemia unawareness. Neuronostatin (NST), a peptide hormone derived from the somatostatin (SST) preprohormone, was discovered by our group in 2008. NST is produced by the same cells as SST, including the pancreatic delta cells. Using the unique Deductive Ligand-Receptor Matching Strategy developed and patented by my lab, we identified the previously orphaned G protein coupled receptor, GPR107, as the putative receptor of NST. We found that NST stimulated glucagon production and release and inhibited glucose-stimulated insulin secretion. Likewise, NST treatment delayed glucose clearance and reduced plasma insulin levels following a glucose challenge, and in addition elevated basal blood glucose levels in semi-fasted animals. We postulate that NST is a novel counterregulatory factor, and that loss of NST signaling following recurrent hypoglycemia contributes to the deficient endocrine responses associated with hypoglycemia unawareness. Our ultimate goals are to determine how NST regulation is impacted by diabetes, and whether NST can be targeted to treat the endocrine deficits associated with recurrent hypoglycemia and hypoglycemia unawareness.

6:30 - 8:30 PM	Transit Zone
POSTER SESSION II	

P1 **Activation Of Vta Ntsr1 Neurons Promotes Weight Loss Behaviors In Obesity**

PATRICIA PEREZ-BONILLA[1,2,3], JILLIAN MATASOVSKY[1,5], SYDNEY PAULS[1,5], GINA M. LEINNINGER[1,4]

[1]Michigan State University, East Lansing, MI, United States, [2]Neuroscience Graduate Program, East Lansing, MI, United States, [3]Pharmacology & Toxicology Department, East Lansing, MI, United States, [4]Physiology Department, East Lansing, MI, United States, [5]College of Natural Science, East Lansing, MI, United States

Dopamine (DA) neurons in the ventral tegmental area (VTA) modulate motivation to engage in physical activity and food intake, behaviors that are disrupted in obesity. Yet, the functional heterogeneity of VTA DA neurons and lack of molecular markers to distinguish them has prevented determination of which DA neurons might be leveraged to support weight loss behaviors. We identified a distinct subset of VTA DA neurons defined by their expression of neurotensin receptor-1 (NtsR1) and hypothesized that they modulate feeding restraint and physical activity. To test this hypothesis, we expressed Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) in the VTA NtsR1 neurons of normal weight and diet-induced obese mice, permitting *in vivo* activation of VTA NtsR1 neurons by treatment with the DREADD-ligand clozapine-N-oxide (CNO). Acute activation of VTA NtsR1 neurons (24 hr) did not alter chow intake, physical activity or body weight in sated, normal weight mice. However, in fasted mice with increased motivation to eat, activating VTA NtsR1 neurons reduced motivated responding for sucrose rewards, and hence, sucrose intake. Likewise, acute activation of VTA NtsR1 neurons in diet-induced obese mice blunted their intake of high-fat diet while increasing their physical activity, an effect that was maintained during chronic (7d) CNO treatment. Thus, activation of VTA NtsR1 neurons during states of high-appetitive drive such as fasting and obesity promotes dual behaviors that support weight loss.

P2 **Central Exendin-4 Selectively Suppresses Cue-Evoked Phasic Dopamine Spikes And Resultant Behavior**

VAIBHAV R KONANUR, TED M HSU, MITCHELL F ROITMAN
University of Illinois at Chicago, Chicago, IL, United States

Cues predicting food reward evoke phasic increases in mesolimbic dopamine activity, appetitive and consummatory behaviors. We have previously shown that the magnitude of cue-evoked dopamine activity scales with hunger or central activation ghrelin receptors. Activation of central receptors for glucagon-like peptide 1 (GLP-1R), via long-acting analogs, suppresses food intake and food motivated appetitive behavior but its effects on cue-evoked, phasic dopamine – a signal critical for reinforcement and goal-directed action – remain unknown. Here, food restricted rats received daily sessions of 30 trials of a tone followed by 1) brief availability of a sipper that delivered 0.3M sucrose and 2) an inter-trial interval. Latency to begin licking and number of licks/trial were measured. After training, rats underwent surgery to express a calcium indicator (proxy for neural activity) selectively in dopamine neurons, implant a fiber optic in the ventral tegmental area and a guide cannula in the lateral ventricle. Following recovery, calcium transients were measured during cue -> sipper sessions. Doses of the GLP-1R agonist, exendin-4 (0, 0.05 or 0.1mg; ICV), were delivered just prior to sessions. While exendin-4 had no effect on spontaneous transient activity, it did dose-dependently suppress the magnitude of cue-evoked dopamine responses (0.39±0.06, 0.27±0.06, 0.04±0.05 DF/F for 0, 0.05 and 0.1mg, respectively; $p < 0.05$). Linear regressions show an inverse relationship between cue-evoked dopamine activity and lick latency and a direct relationship with number of licks/trial. As cue-evoked dopamine promotes approach and consumption, exendin-4 may be therapeutic in suppressing neural substrates involved in cognitive and reinforcement related overeating.

P3 **Reduction In Heroin Taking And Seeking Induced By Glucagon-Like Peptide-1 (Glp-1) Analogs Is Accompanied By Changes In The Expression Of &Lsquo;Satiety&Rsquo; Genes In &Lsquo;Reward&Rsquo; Nuclei In Rats**

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[1]Department of Neural and Behavioral Sciences, Penn State College of Medicine, Hershey, PA, United States, [2]Department of Pharmacology, Penn State College of Medicine, Hershey, PA, United States

Drugs of abuse alter the normal functioning of the brain reward system and direct focus toward drug seeking and drug taking. Indeed, the motivated state of an individual when craving drug is similar to the state observed in animals that crave food when hungry, water when thirsty, or salt when sodium deficient. There is only one goal and there is no substitute. Recent evidence shows that hormones that regulate feeding motivated behaviors, such as GLP-1, also can modulate non-feeding motivated behaviors associated with drugs of abuse such as alcohol, nicotine, or cocaine. Here we show that systemic administration of the GLP-1 analog exendin-4 (Ex-4) increases acceptance of a heroin-paired natural reward, decreases cue-induced heroin seeking, and decreases heroin-induced reinstatement of heroin seeking behavior (i.e. relapse) in rats. Likewise, systemic administration of the longer-acting GLP-1 analog, liraglutide, also decreases drug taking and relapse. Following cue-induced reinstatement, rats in the Ex-4 study were sacrificed and different brain regions were obtained to assess gene expression changes using qPCR. In the nucleus accumbens shell (NACsh), chronic treatment with Ex-4 reduced expression of leptin receptor and EGR2, and increased expression of orexin receptor 1. In addition, Ex-4 increased expression of GLP1R, b-catenin, CRHR2 and CRH binding protein in NACsh of the most vulnerable population. Taken together, these data support the notion that drug addiction alters both the reward and the need

system as the behavioral effects induced by Ex-4 treatment are associated with changes in the expression of genes involved in hunger and satiety (e.g., leptin and orexin receptors) in a key structure of the reward pathway

P4 **Effects Of 6-Hydroxydopamine Lesions Of The Substantia Nigra, The Dorsal Striatum, The Medial Accumbens And The Lateral Accumbens On Free-Choice High-Fat High-Sugar Diet Component Preference**

ANIL JOSHI[1,2,3], FANNY FAIVRE[1], TESS KOOL[2,3], LAURA L. KOEKKOEK[2,3], CHARLENE DIEPENBROEK[2,3], JORAM D. MUL[2,3], IPEK YALCIN[1], SUSANNE E. LA FLEUR[2,3], MICHEL BARROT[1]

[1]CNRS, Université de Strasbourg, Institut des Neurosciences Cellulaires et Intégratives, Strasbourg, France, Strasbourg, France, [2]Amsterdam University Medical Center, University of Amsterdam, Department of Endocrinology and Metabolism & Laboratory of Endocrinology, Department of Clinical Chemistry, Meibergdreef 9, 1105 AZ, Amsterdam, Netherlands, Amsterdam, Netherlands, [3]Metabolism and Reward Group, Netherlands Institute for Neuroscience, Institute of the Royal Netherlands Academy of Arts and Sciences (KNAW), Meibergdreef 47, 1105 BA, Amsterdam, Netherlands, Amsterdam, Netherlands

Dopamine (DA) signaling regulates feeding-related behavior. Conversely, caloric intake, especially of palatable dietary items, can modulate function of the DA-related brain circuitry. For example, it has been observed that increased intake of dietary fat results in blunted DA signaling, and, to compensate for this lowered DA function, caloric intake may subsequently increase. To determine how DA signaling regulates food preference, we utilized 6-hydroxydopamine (6-OHDA)-mediated lesioning to deplete DA-related signaling in specific brain regions of male Sprague Dawley rats. Food preference was then assessed by providing the rats with a free-choice four-component high-fat high-sucrose [fc-HFHS; a container of prefabricated control diet (CD), a dish of beef tallow, a bottle of tap water, and a bottle of 30% sucrose solution] diet. Rats with lesions of the substantia nigra (SN; which also offer a model of Parkinson's disease) consumed less calories ($P < 0.05$), reflected by a decrease in CD intake ($P < 0.05$), an increase in fat intake ($P < 0.05$), but without changes in sucrose solution intake compared to non-lesioned controls . To determine which of the SN projection areas contributes to these effects, we next compared 6-OHDA lesions targeted to DA neuron terminals in the dorsal striatum, the medial nucleus accumbens (NAc) or the lateral NAc. We observed that 6-OHDA lesioning of the lateral NAc, but not the dorsal striatum or medial NAc, led to increased fat intake ($P < 0.05$). These findings indicate a role for DA signaling in the lateral NAc in regulating food preference, in particularly the intake of fat.

P5 **Shock-Paired Conditioned Stimuli Induce Freezing And Suppress Palatable Food Intake Through Separable Neural Pathways**

CAITLYN M EDWARDS, LINDA RINAMAN
Florida State University, Tallahassee, FL, United States

Defensive, appetitive, and other competing motivational drives coordinate behaviors essential for survival of animals. Previous studies indicate that environmental conditioned cue and contextual stimuli (CSs) compete with homeostatic motivational signals by enhancing food intake in sated rats or inhibiting food intake in food-deprived rats, depending on CS pairing history with appetitive or aversive unconditioned stimuli (USs). The present study extends these results by exploring how CSs paired with an aversive mild electric footshock US compete with hedonic motivational signals. For this purpose, rats received either paired or unpaired tone-footshock training in a novel context. Rats were later re-exposed to the shock context or to the shock-paired tone cue, with concurrent access to highly palatable FrootLoops. Shock-paired contextual and tone cues each suppressed appetitive FrootLoop consumption and increased defensive freezing behavior (subject to extinction after multiple re-exposures), evidence that fear CSs compete with hedonic motivational drive. Additionally, since previous reports indicate that vagal sensory stimuli can enhance associative fear memory consolidation in avoidance paradigms, we examined whether pharmacological activation of vagal afferents using cholecystokinin (CCK; 1 μg/kg BW) immediately after a shock-CS conditioning session enhances fear-CS learning. Initial results indicate that post-conditioning CCK treatment increases FrootLoop intake during re-exposure to the CS despite similar or enhanced CS-induced defensive freezing behavior, suggesting that vagal sensory signals differentially impact the neural circuits that mediate these two types of motivated behavior.

P6 **The Effects Of Combined Transection Of The Chorda Tympani And Glossopharyngeal Nerves In C57Bl/6J, 129X1/Svj, And T1R2+T1R3 Knockout Mice On Responsiveness To Maltodextrin And Sucrose In A Brief Access Test.**

CHIZUKO INUI-YAMAMOTO[1,2], GINGER D. BLONDE[1], TADASHI INUI[1], ALAN C. SPECTOR[1]

[1]Department of Psychology and Program in Neuroscience, Florida State University, Tallahassee, FL, United States, [2]Department of Oral Anatomy and Developmental Biology, Osaka University Graduate School of Dentistry, Suita, Japan

Knockout (KO) mice lacking the "sweet" taste receptor T1R2+T1R3 display concentration-dependent behavioral responses to maltodextrin solutions, such as Maltrin, in taste tests. The sources of this T1R-independent mechanism remain unclear. Here, we examined the necessity of lingual taste fields in maintaining maltodextrin responsiveness. C57BL/6J (B6), 129X1/SvJ (129), and T1R2+T1R3 KO male and female mice received either sham surgery (SHAM) or had bilateral transections of the chorda tympani (CT) and glossopharyngeal (GL) nerves (CTX+GLX). After presurgical training, fasted (~22.5h) mice were given a series of 30-min brief access tests (10-s trials) using Maltrin (1-32%) before and after surgery, and then sucrose (1-32%). Concentration-dependent increases in licking of Maltrin and sucrose were blunted (all Ps< .01) after CTX+GLX in B6 (n=13) and 129 (n=14) mice relative to sham-operated controls (B6, n=14; 129, n=14). There were no significant differences between SHAM (n=16) and CTX+GLX (n=16) KO mice; both surgical groups increased

responsiveness to Maltrin with concentration and, as expected, had severely blunted responsiveness to sucrose. These results confirm the primacy of T1R2+T1R3, and demonstrate the necessity of the lingual taste nerves, in the maintenance of normal concentration-dependent licking to sucrose in mice. The decrease in licking to Maltrin after CTX+GLX in B6 and 129 mice is likely due to the presence of low molecular weight saccharides in the solution, a finding supported by the lack of a surgical effect in KO mice. The responsiveness to Maltrin in KO mice and the residual responsiveness to sucrose in wild type mice after CTX+GLX are possibly due to palatal taste receptors innervated by the greater superficial petrosal nerve.

P7 **Denatonium Diet Alters Salivary Protein Expression.**

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We have previously demonstrated that a subset of salivary proteins (SPs) are upregulated in rats after exposure to a tannic acid diet (TA, 3%) or a quinine diet (0.375%) but SP expression was not changed after exposure to a concentration of sucrose octacetate (SOA, 4%) that resulted in a similar reduction in 24-h food intake. We have also demonstrated that animals with these SPs upregulated increase acceptance of quinine, but pre-exposure to SOA did not. In this study we chose to examine if denatonium benzoate (DB) alters SP expression. It is a commonly used bitter in both taste research and has real world applications as an aversive bitterant. We fed animals 0.85% DB diet for 14 days (n=4). Rats decreased 24-h food intake, meal size and rate of feeding (p's < 0.005) during first 4 days of exposure followed by an increase in 24-h intake, meal size, and rate of feeding returned to near baseline levels. Following a brief recovery period (6-days on a control diet), animals were fed a 0.375% quinine diet. Rats who had previously been exposed to the DB diet had a higher rate of feeding and consumed more quinine diet than control animals. Five out of seven of the bands containing the SPs that were upregulated by TA and quinine were also upregulated by denatonium (35, 23, 19, 18.5, and 13 kDa). These data suggest that the proteins that are altering the acceptance of quinine are in this set of bands.

P8 **Bitter Stimuli Differ Qualitatively In Humans**

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Bitterness is assumed to be a marker of toxicity. That is, stimuli humans describe as bitter are innately aversive, and stereotypical rejection responses are conserved across species, presumably to prevent toxin ingestion. However, this is an oversimplification as recent chemoinformatic analyses suggest only 60% of stimuli in the BitterDB database are toxic, and only 56% of toxic compounds are expected to be bitter. Working from the premise that bitterness is a marker of pharmacological activity rather than toxicity, we have explored whether different bitterants are perceptually distinct in humans, despite the absence of semantic labels for such differences. In study 1, 36 naïve assessors were asked to taste intensity matched bitterants and group them on the basis of similarity in a free sorting task. We found 3 clusters: a quinine/naringin cluster, a caffeine/theobromine/SOA cluster, and a tetralone/urea/L-tryptophan/L- phenylalanine cluster. In study 2, 63 participants tasted 3 bitterants in a whole mouth sip and spit task, rating the intensity at 5 loci. In study 3, an experimenter painted 2 bitterants on the fungiform, circumvallate, and foliate papillae with a cotton swab in 48 participants, who rated the intensity at each locus. In both, the locus by bitterant interaction was significant, driven mainly by reduced intensity for tetralone, a hop extract, on the anterior tongue. In study 4, 14 trained assessors rated 10 bitterants in a time intensity task. Differences were observed for time to maximum; also intensity of some bitterants increased substantially after swallowing while the intensity of other bitterants did not. These data support the idea that different bitter stimuli are perceptually distinct in humans, possibility due to effects of timing and location.

P9 **Towards Understanding Differences In Oral Processing Behaviour Between Asian, Chinese And Caucasian, Dutch Consumers: A Physiological Perspective**

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Oral processing behaviour is known to differ between consumers groups leading to differences in sensory perception. Differences in food oral processing behaviour between consumers of different ethnicities or gender may be explained by differences in oral physiology and psychological factors. This study aims to explore the oral physiological differences of consumers varying in ethnicity, and secondly establish the relationship between oral physiology and oral processing behaviour. Dutch Caucasian adults (18-30 years, n=36) and Chinese Asian adults (18-30 years, n=36) were recruited. Oral physiology of all consumers was characterized by salivary flow rate, volume of oral cavity, mastication efficiency, tongue dimensions and dental status. The oral processing behaviour (consumption time, bite size, eating rate, number of chews) was assessed by video recording the consumption behaviour of the subjects, while consuming a carrot, cheese and sausage sample. Asian, Chinese consumers took smaller bites, had longer consumption times resulting in lower eating rates compared to Caucasian, Dutch consumers. Mastication efficiency was higher in Asian, Chinese than Caucasian, Dutch consumers. Oral cavity volume did not differ between Asian, Chinese and Caucasian, Dutch consumers. These physiological parameters only explain the variation in oral processing behaviour to a limited extend. This suggests that other physiological and psychological factors contribute more to oral processing behaviour. This study found physiological differences between Asian, Chinese and Caucasian, Dutch consumers. However, a link between these physiological parameters and oral processing behaviour has not been found yet.

P10 **Anthropometric And Psychological Correlates Of Following A Vegetarian Diet: A Large Cohort Cross-Sectional Approach**

EVELYN MEDAWAR[1,2,3], STEFFI RIEDEL-HELLER[4], ARNO VILLRINGER[1,2,3], A. VERONICA WITTE[1]

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Meat-restrictive eating patterns such as vegetarian and vegan diets have been suggested to convey health benefits for cardiovascular risk factors, e.g. weight status (1–4). However, recent studies indicated conflicting evidence for emotional health, including higher depression in vegetarians (5–8). We aimed to systematically investigate those potential effects in a large population-based sample. Self-reported food frequency, body-mass-index (BMI) and neuropsychological questionnaires were assessed in 1213 (532F) participants of the LIFE-Adult-Study (9) (age 19-80 years, mean BMI=27.1±4.5). A composite score for the frequency of animal-derived food intake was calculated based on (processed) meat, sausage, , fish, dairy and egg intake over the last year). In linear regression models, lower frequency of animal product intake was significantly associated with lower BMI, higher depressive symptom scores and higher neuroticism, extraversion and openness, explaining a small amount of variance (all $|ß| > 0.05$, all $p < 0.033$, all $R2 > 0.03$)). When adjusting for age, sex and education, however, results remained stable for BMI ($ß = 0.07$, $p = 0.018$) and openness personality trait only ($ß = 0.07$, $p=.016$) This cross-sectional study shows that lower animal product eating behaviours are weakly associated with lower BMI and trait openness in a large population-based sample of adults. Limitations include the self-reported measures which might be prone to over- or underestimation, and the associative-only nature of our cross-sectional design. Future longitudinal studies need to disentangle potential mechanisms between dietary habits, anthropometrics and personality as proposed by the current study.

P12 **Diet And Metabolic System Influences On The Ageing Brain: Preliminary Results Of A Systematic Review**

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Diet and metabolism can influence brain health over the lifespan. These variables affect quality of life and the chances of developing risk factors for dementia such as obesity or type-2-diabetes. Identifying indicators of brain health, such as brain areas and connectivity patterns that are related to diet and metabolism, is thus an important step in understanding healthy brain ageing. This systematic review and meta-analysis aims to identify, classify, and analyze the available literature examining associations of diet and metabolism with brain health. The function of specific brain connections will be related to cognitive performance in reviewed studies. Searches were performed from October 2018 onwards in MEDLINE, Pubmed, Ovidsp: EMBASE and PsycINFO, yielding 2281 publications in total. The search was conducted for all keywords on diet/metabolism, brain changes and ageing. Inclusion criteria included the report of any kind of association between brain areas and/or connections and diet and/or metabolism. Exclusion criteria included animal studies, a lack of data on participant age, and non-English publications. Random-effect meta-analysis will be performed to calculate pooled effect sizes and 95% CIs. The analysis is currently ongoing; however, a preliminary summary of the literature suggests that objectively indicators of healthy diet and metabolism may be related to increased structural volume and resting-state fMRI activity in the hypothalamus, hippocampus, and some brainstem areas. Only a few studies report effects of those health indicators on brain networks. This study offers preliminary support for an association between diet and metabolism and healthy brain ageing, and highlights a current lack of research on brain connectivity between key areas.

P13 **Mice Have Reduced Meal Number And Meal Size At Cage Temperature Of 28°C Versus 21°C**

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Studies on energy balance regulation in mice are typically performed at standard room temperature of 21 °C. Because this is below thermoneutrality, a substantial part of the energy intake is used for maintenance of body temperature, which in turn would affect ingestive behavior. To investigate this, we analyzed meal patterns of 3 months old male C57Bl6/J mice solitarily living from weaning onwards at 21°C or 28°C, feeding either a 5.5% low fat (LF) diet or an obesogenic diet consisting of 40% fat and sucrose (HFS diet). Ingestive behavior was studied using a TSE automated recording system assessing food intake to the nearest 0.04 gr every 10 sec over a period of 6 days. Mice feeding the HFS diet were heavier compared to LF feeding mice, however, body weights at the two temperatures were exactly the same. As expected, daily caloric intake was significantly higher (appr 5kcal/day) at 21°C than at 28°C, and higher (appr 2 kcal/day) in HFS fed mice than in LF fed mice. Using log survivor analysis for each animal, we calculated breaking points yielding intermeal-intervals that were significantly shorter for mice at 21°C than at 28°C, and shorter in mice on the HFS diet compared to the LF fed mice. Meal frequency was consistently higher at 21°C than at 28°C, and higher in HFS fed mice versus LF fed mice. The accompanying meal sizes were reduced in mice at 28°C versus 21°C, however, they were not affected by diet. Based on similar bodyweights of mice at 28°C versus 21°C, it is concluded that the excess energy intake at 21°C is required for thermogenesis, and that an increase in meal size as well as meal number contributes to

these effects. Excess energy intake in HFS fed mice underlies body weight gain, with higher meal frequency mainly contributing to this effect.

P14 **Sex Differences In Meal Patterns In Response To Exercise**

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Preclinical data from our lab consistently shows that exercise (EX) counters the biological drive to regain lost weight in male but not female rats. These sex-differences are largely driven by differences in food intake in response to the exercise. We recently set out to replicate our work in rats without a history of weight loss. Briefly, rats were housed in metabolic cages & fed ad libitum for 6 weeks prior to randomization to sedentary (SED) or EX groups. EX rats completed 1 hour of treadmill exercise 5 days/week at 15m/min for 4 weeks. Prior to the start of EX and during the last two weeks of EX training, food intake was evaluated using the BioDAQ food monitoring system. Consistent with our prior work, EX acutely reduced food intake over 24 hours in male rats and acutely increased food intake in female rats. When the data were analyzed as the difference between pre and post EX, then separated into the light (14hr) and dark cycle (10 hr), we observed that males and females differentionally adjust feeding behavior in response to EX. The decrease in food intake in males occurred during the dark cycle (SED: -9.7 ± 2.4 EX: -19.1 ± 1.9 kcals, $p < 0.05$) and corresponded with a decrease in meal number (SED: -0.4 ±0.3 EX: -1.6 ± 0.3, $p < 0.05$), and an increase in the post meal interval (SED: -343 ± 663 EX: 3536 ± 968 s, $p < 0.05$). The increase in food intake in female rats in response to exercise primarily occurred during the light cycle (SED: 5.0 ± 1.3 EX: 11.2 ± 1.6 kcals, $p < 0.05$) with an increase in meal size (SED: -0.8 ± 0.5 EX: 0.7 ± 0.3 kcal/meal, $p < 0.05$) and rate of consumption (SED: -1.6 ± 0.5 EX: -0.4 ± 0.8 s, $p < 0.05$). These sex specific differences in meal patterning may help uncover the mechanisms driving the sex difference in appetite in response to exercise.

P15 **Effects Of Voluntary Wheel Running On Free-Choice High-Fat High-Sugar Diet Component Preference**

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Overconsumption of high-caloric palatable diets (HPDs), enriched with processed fat and sugars, is a strong driver of the global obesity epidemic. Conversely, exercise training increases general health and promotes body weight control. In humans and rodents, exercise training also alters dietary choice and/or diet component preference, suggesting that changes in dietary preference contribute to the exercise training responses on body weight. Nonetheless, the central molecular mechanisms underlying changes in dietary preference remain poorly understood. To model the effects of exercise training on diet choice in humans pre-exposed to obesogenic multi-component HPDs, male Wistar rats were fed a free-choice four-component high-fat high-sucrose [fc-HFHS; a container of prefabricated control diet (CD), a dish of beef tallow, a bottle of tap water, and a bottle of 30% sucrose solution] diet or a no-choice CD, and diet component preference and metabolic behavior was assessed during both sedentary (SED) and voluntary wheel running (VWR; self-reinforcing rodent behavior that mimics aspects of human exercise training) conditions (n=18/group). At sacrifice, several brain areas were isolated for RT-qPCR analyses. VWR transiently lowered caloric intake, blunted body weight gain, and decreased terminal fat mass, independent of diet, compared to SED rats. $VWR^{fc\text{-}HFHS}$ rats showed a consistent higher preference for CD, a transient lower preference for fat, but no clear effects on sucrose solution preference, compared to $SED^{fc\text{-}HFHS}$ rats. We are currently correlating the expression of dopamine- and opioid-related genes in the lateral hypothalamus and the nucleus accumbens, brain regions involved in the control of reward-driven and metabolic behavior, to these behavioral observations.

P16 **Brain Region And Sex Specific Changes In Expression Of Genes Involved In Glucocorticoid Signaling In Running-Induced Changes In High Fat Diet Preference**

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When access to wheel running (WR) and a two-diet choice, a standard high carbohydrate chow vs. a palatable high fat (HF) diet, feeding regimen are introduced simultaneously, rats decrease their HF diet intake and preference to the extent of complete avoidance. With continuous running, most male rats maintain such avoidance beyond two weeks whereas the majority of females reverse the avoidance to preference within the same period. Given that WR activates the hypothalamic-pituitary-adrenal axis and increases glucocorticoid levels, we investigated how glucocorticoid signaling is involved in the sex-dependent, running-associated HF diet avoidance in two studies. The first study revealed that adrenalectomy had little influence on the initiation and maintenance of running-induced HF diet avoidance in male rats. In the second study, expression of genes involved in glucocorticoid signaling (*Nr3c1, Src1, Ppid, Fkbp5 & bag1*) in the paraventricular nucleus of the hypothalamus (PVN), hippocampus (HP), and prefrontal (PFC) and insular cortex (IC) of sedentary and WR male and female rats with two-diet choice was assessed using RT-PCR. The results revealed few significant group differences in the PVN and HP. By contrast, WR rats had increased expression of *Fkbp5* in both the PFC and IC, and Ppid in only the IC. Intriguingly, male and female WR rats had different profiles of *Nr3c1* expression

in the two areas depending on whether they maintained HF diet avoidance – only females that maintained and males that reversed HF diet avoidance had increased *Nr3c1* expression. Taken together, the sex-dependent running-associated diet choice patterns and glucocorticoid-related gene expression profiles may underlie sex differences in the beneficial effects of exercise on physical and mental health.

P17 **Activation Of Brown Adipose Tissue Thermogenesis In Response To High-Fat/Sugar Choice Diet Challenge Is Dictated By Sex.**

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Women and men have different patterns of illness and they respond differently to pharmacotherapies. Obesity is more prevalent in women compared to men, and women are more likely to develop morbid obesity, according to NIDDK. Preclinical studies designed to not only determine whether there are sex differences in commonly used rat models of obesity, but also aiming to pursue the identified differences mechanistically are still lacking. Therefore, the main aim of this study was to 1) determine whether time course and presentation of diet-induced obesity differs between male and female rats, and 2) investigate the mechanisms underlying potential differences. To achieve this, male and female rats were offered a choice of a high-fat/high-sugar (HFHS) diet and regular chow for 12 weeks. Body weight gain, food intake, fat mass, and brown adipose tissue thermogenesis were measured. The extent of overconsumption was similar in males and females offered a choice of HFHS and chow, compared to control rats offered only chow; the impact of that overconsumption on weight gain and blood sugar differed significantly. While females started gaining weight immediately, males were protected from weight gain until 10 weeks on the diet, suggesting that males were able to engage compensatory energy expenditure strategy. In line with this idea, we found that HFHS-fed males, but not females, displayed a clear and potent diet induced thermogenesis driven by activation of brown adipose tissue. We are now pursuing the molecular mechanisms of this sex divergent response to HFHS diet challenge, including potential differences in sympathetic activation of brown adipose tissue and ability to engage white fat browning. These data may also suggest that sex specific weigh loss therapies should be considered.

P18 **Exercise Improves Brain Insulin Action And Executive Function In Adults With Overweight And Obesity**

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Exercise has beneficial effects on metabolism and brain function. However, little is known whether exercise can improve insulin sensitivity of the brain. In the current study, 22 participants with overweight and obesity (BMI 31.15±3.87 kg/m^2 and age 30.41±8.6 years) underwent two functional magnetic resonance imaging (fMRI) sessions before and after an 8-week supervised exercise intervention, including cycling and walking training. During the fMRI session, intranasal insulin was used to probe brain insulin action. Furthermore, participants were assessed for cognition, mood, peripheral insulin sensitivity, and mitochondrial energy metabolism of the skeletal muscle. We observed exercise-induced increase in cerebral blood flow in the cerebellum, midbrain, thalamus and hypothalamus. In response to intranasal insulin, participants showed an increase in striatal blood flow prior to the intervention and a decrease after the intervention. This insulin-driven attenuation is consistently observed in healthy individuals. Interestingly, the exercise-induced 'normalized' brain insulin action correlated with improved peripheral insulin sensitivity and mitochondrial energy metabolism. Participants who improved their peripheral metabolism showed the most prominent change in brain insulin action and better dopamine-dependent executive functioning based on the trail-making test after the exercise program. Exercise significantly improved brain insulin action, which was related to improvements in whole-body metabolism. As not all participants showed this beneficial effect on insulin action, methods to boost brain insulin sensitivity are needed to improve glucose metabolism and brain functions.

P19 **Physical Inactivity Reduces ΔFosb In The Stress- And Reward-Related Brain Circuitry Of Male Wistar Rats**

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In recent decades, the average lifestyle has become increasingly less active. This has a negative impact on general health and well-being. Conversely, exercise training (i.e. repeated bouts of physical activity) promotes health across diverse organ systems. For example, exercise training improves brain plasticity and has beneficial effects on several brain-related disorders, including major depressive disorder. Despite the clinical importance of these effects, the underlying molecular mechanisms are poorly understood. We use voluntary wheel running (VWR), self-reinforcing behavior that mimics aspects of exercise training, to gain insight into the multiplicity and complexity of neuronal networks involved in exercise training responses. Here, we focused on the stress- and reward-related brain circuitry and compared activation of neurons in this circuitry in male Wistar rats housed without (sedentary) or with a running wheel for 28d (1.55±0.2 km of voluntary exercise per day; n=12/group). Immunocytochemical quantification of ΔFosB, a stable protein that accumulates during persistent activation of a neuron, was used as a proxy of neuronal activation. Compared to VWR rats, sedentary rats had significantly lower ΔFosB immunoreactivity in (subregions of) the striatum, cortex, hippocampus, amygdala, and hypothalamus ($P < 0.05$). These findings indicate lower activation of several key hubs of the stress- and reward-related brain circuitry during sedentary housing. Because ΔFosB is a transcription factor that regulates transcription of hundreds of target genes, our findings indicate widespread perturbations in neuronal activation and function during a sedentary lifestyle. Follow-up studies will investigate the functional and behavioral consequences of these perturbations.

P20 **Food Intake And Eating Behavior During A Real-Life Snack Situation In Children And Adolescents With Obesity (Obe) Before And After Weight Loss Compared To Controls With Normal Weight (Nw) &Ndash; An Experiment Using A Hidden Camera.**

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The objective was to investigate changes of food intake and eating behavior in OBE during an inpatient weight reduction treatment in comparison to NW, in a real-life snack situation. Sixty OBE were examined before (T1) and after weight loss (T2); 27 NW were examined once, as control group (age: 9-17). The snack situation took place after psychophysiological measurements. Children were invited to relax and watch a film for 20 minutes and to eat *ad libitum* foods with varying energy density from a plate before leaving the room. A dividing wall was arranged between the investigator's desk and the seated child. Food intake was assessed by a precision scale, eating behavior by hidden camera. The food amount and energy intake increased from T1 (144±106g, 260±211kcal) to T2 (187±91g, 369±202kcal) in OBE (each p< .001) but did not differ to NW (155±83g, 255±175kcal) at T1. The latency of food intake decreased from T1 (1:11±2:57min) to T2 (0:26±01:00min, p< .001) but was longer compared to NW (0:07±00:08, p< .001) at T1. NW touched the food more often than OBE but the rate of moving food to the mouth was similar. To identify within-session changes, we segmented the sessions into four 5 minute intervals. At T1, OBE and NW showed a linear decrease in eating occasions (0.7 fewer occasions every 5 min, p< .001). Intake increased from T1 to T2 (0.8 more occasions), while the within-session decrease also accelerated (1.2 fewer occasions every 5 min.; interaction segment*session, p< .001). Subanalyses show that the second result is due to increased intake of high energy foods. Energy intake was similar in NW versus OBE at T1 but eating behavior differed. The increased energy intake of OBE at T2 may be a compensatory behavior to counteract the weight loss.

P21 **Exploring Rodent Models Of Maternal Obesity And Its Effects On The Metabolic Health Of The Dam**

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Paralleling the global rise in obesity, it is estimated that up to 30% of pregnant women worldwide are overweight or obese, which increases short- and long-term adverse health outcome for both the mother and child. While numerous studies have used rodent models of maternal obesity to better understand its pathophysiological consequences on long-term health, most have done so to assess the intergenerational effects on the offspring, and characterization of changes in the dams is sparse. Women who are overweight or obese during pregnancy are at a higher risk for developing both metabolic and mental disorders, like gestational diabetes and postpartum depression. In order to investigate the relationships between maternal obesity and the mother's health, we have begun to characterize a rat model of maternal obesity based on a polygenic predisposition for obesity (obesity-prone; OP), which is exacerbated by access to a sweetened, high fat diet (HFD). The OP dams maintained on HFD gained significantly more weight during pregnancy and were slower to lose weight during lactation than chow-fed dams (P< 0.001). OP-HFD dams also exhibited impaired glucose tolerance during pregnancy and lactation (P< 0.001), and ingested more calories than chow-fed dams during early pregnancy (P< 0.05) and throughout lactation (P< 0.05). Leptin levels were higher in OP-HFD than chow-fed dams before, during, and after pregnancy (P< 0.001), but insulin levels were lower before and after pregnancy. In liver tissue collected at 3-weeks postpartum, often severe lipidosis was observed in OP-HFD dams, but not chow-fed dams. The metabolic profile of the OP-HFD dams demonstrates the usefulness of this model for studying maternal obesity, and warrants further metabolic, behavioral, and neural characterization.

P22 **Differences In Birth Weight Predict Food Preferences In Siblings**

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Background/ Aim: Low Birth Weight (LBW) is implicated in the risk for adult conditions such as increased abdominal fat and metabolic disorders. We have shown that lower birth weight is associated with preference for palatable foods at different ages, which may contribute for the metabolic disarrangements seen in adults. However, it is not clear the role that the family environment has on this process. Our objective was to investigate if a lower birth weight is associated with specific food preference between siblings of the same family. Methods: 61 sibling pairs from the cities of Montreal and Hamilton (CA), were recruited from an established prospective birth cohort (Maternal Adversity, Vulnerability and Neurodevelopment – MAVAN - project). At 48-months of age, mothers completed a Food Frequency Questionnaire. Analyses were performed considering each child of a sibling's pair in one group, so that environmental influences could be controlled. Generalized Estimating Equations were used to evaluate the effect of birth weight (smaller X higher) on food preferences at 4 years of age, adjusted by birth order, sex and BMI. Results: Lower birth weight was related to smaller percentage of protein intake (M=17.9, EP=0.42 X M=19.0, EP=0.46, p=0.027) and to an increased carbohydrate-to-protein ratio: M=3.1, EP=0.12 X M=2.8, EP=0.11, p=0.038). There were no differences between groups for total calories consumed per day (p=0.299), % carbohydrates intake (p=0.455) and % fat intake (p=0.892). Conclusions: These findings are observed within the same family, which reinforces that the association between lower birth weight and increased preference for carbohydrates over protein is more biologically-driven rather than an environmentally-based variation, and can be observed early in life.

P23 **Maternal High Fat Diet During Gestation Alters Circulating Exosome Mirna Signature In The Rat.**

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The intrauterine environment supports fetal growth and development and alterations to this environment can have long-lasting adverse effects on the health of offspring. Offspring of rat dams fed a 60% high fat diet (HFD) during gestation and lactation have increased risk for diet-induced obesity, impaired glucose tolerance, and cognitive deficits compared to offspring of chow control diet (CD) dams. Exosomes are small nanovesicles (< 200 nm) that are released by cells into circulation and carry bioactive molecules, such as miRNA, mRNA, or protein, that can be delivered to distant cells to modify their function. Exosomes represent a mode of communication between mother and fetus that can alter offspring development *in utero*. Exosome miRNAs, small noncoding RNAs that regulate post-transcriptional gene expression, in plasma of pregnant rat dams are a potential mediator of the negative phenotypic outcomes associated with maternal HFD consumption during gestation. Plasma was collected from pregnant dams fed CD or HFD (n=8/diet) on gestation day 21 to isolate circulating exosomes. Non-pregnant female rats were included as additional controls (n=8). miRNA-enriched total RNA was isolated from exosomes and sequenced using the Illumina platform. Plasma exosome number was 2-fold higher in pregnant vs. non-pregnant rat dams, independent of diet. A total of 61 miRNAs, including members of the let-7 family, were upregulated in HFD dams compared to CD dams. Higher expression of the miR-let-7 family has been associated with impaired glucose metabolism, insulin resistance, and altered neural development. Exosomes and their cargo can influence fetal development and could be a target for improving offspring health in the face of *in utero* stress, such as altered maternal nutrition.

P24 **Timing Of Eating And Demographic, Pregnancy-Related, And Weight-Related Factors During Early Pregnancy**

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Emerging evidence suggests that circadian timing of eating (i.e., when individuals eat) plays a key role in weight and health. However, little is known about circadian timing of eating in pregnancy, a unique period in which women's eating patterns change. We sought to describe the circadian timing of eating and associations with demographic, pregnancy- and weight-related factors among pregnant women with overweight/obesity. Women (*N*=165; 45% non-White) between 12-20 weeks gestation with a prepregnancy body mass index (BMI[kg/m^2])≥25 were recruited for a perinatal weight study. At baseline, women completed 24-hour dietary recalls, which yielded two measures of circadian timing of eating: length of eating window (difference in time between first & last meal within one 24-hour period); and mid-eating time (mid-point of eating window, indicating when it occurred in the 24-hour period). Women reported demographic and pregnancy-related factors, and weight and height were obtained via calibrated scale and stadiometer. Correlations and *t*-tests were conducted. Pregnant women had an eating window lasting 11.2±3 hours and mid-eating time of 14.7±2 hours after midnight (approximately 2:40pm or 14:40). A longer eating window and earlier mid-eating time were related to higher age (*r*s>.2, *p*s< .01) and reporting on a weekday vs. weekend (*t*s(168)≥2.0, *p*s< .04). Mid-eating time was earlier in White vs. non-White women (*t*(167)=3.9, *p*< .01) and women with a household income above vs. below $30,000 (*t*(168)=3.6, *p*< .01). Eating window length and mid-eating time were not related to gestational age, BMI, parity, employment or relationship status (*p*s>.11). Our results highlight the importance of assessing eating timing in future research with pregnant women across the weight spectrum.

P25 **Nts Mc4R Activation Is Associated With Nmdar-Dependent, Sustained Enhancement Of Cck-Induced Reduction Of Food Intake**

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Previously we reported that reduction of food intake following injection of the melanocortin 4 receptor (MC4R) agonist, MTII, into the nucleus tractus solitarius (NTS) is attenuated by co-injection of an N-methyl-d-aspartate glutamate receptor (NMDAR) antagonist. We postulated that this reduction of food intake might reflect sustained enhanced responsiveness to gastrointestinal satiation signals, such as cholecystokinin (CCK), and that this enhancement might be mediated by NMDAR-dependent processes in the NTS. To test these hypotheses, we injected MTII (20 ng) or vehicle unilaterally into the NTS of ad libitum-fed rats at 0900h (lights on 0700 and off at 1900). Then, 4.5h n=10) or 6h (n=10) later, at 1330 or 1500h, the rats were injected IP with either 0.9% NaCl or CCK (0.25 μg/kg), immediately prior to measuring their 30 min consumption of a 15% sucrose meal. We found that NTS MTII followed 4.5 or 6h later by IP NaCl reduced 15% sucrose consumption by 26±8% and 31±5% respectively. Following NTS vehicle injection, IP CCK produced non-significant (6±12% or 8±12%) reductions of sucrose intake 4.5 and 6h post-injection. However, when CCK was injected 4.5 or 6h after NTS MTII, 30 min sucrose intakes were reduced by 61±4 and 79±6% respectively. These reductions were significantly greater than those produced by either MTII or CCK separately. Finally, when an NMDAR antagonist was co-administered into the NTS with MTII, subsequent reduction of sucrose intake by CCK was significantly attenuated. Our results suggest that hindbrain MC4R activation triggers an increase in responsiveness to CCK lasting for at least 6h, and that neural changes that mediate increased response to CCK might represent NMDAR-dependent neuroplastic changes in the NTS.

P26 **Critical Role Of Parabrachial Interleukin-6 In Energy Metabolism**

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Chronic low-grade inflammation and increased serum levels of the cytokine IL-6 accompany obesity, but mechanisms by which brain-produced IL-6 controls energy balance, and their role in obesity remain unclear. Here, we show that, brain-produced IL-6 was decreased in obese mice and rats, in a neuroanatomically and sex-specific manner. Reduced IL-6 mRNA localized to lateral parabrachial nucleus (lPBN) astrocytes, microglia, and neurons, including paraventricular hypothalamus-innervating lPBN neurons. IL-6 microinjection into lPBN reduced food intake and increased brown adipose tissue (BAT) thermogenesis in male lean and obese rats by increasing thyroid and sympathetic outflow to BAT. Parabrachial IL-6 interacted with leptin to reduce feeding. siRNA-mediated reduction of lPBN IL-6 led to increased weight gain and adiposity, reduced BAT thermogenesis, and increased food intake. Ambient cold exposure partly normalized the obesity-induced suppression of lPBN IL-6. These results indicate that lPBN-produced IL-6 regulates feeding and metabolism, and pinpoint patho/physiological contexts interacting with lPBN IL-6.

P27 **Binge-Like Food Intake Decreases Preproglucagon Mrna Expression In The Nucleus Tractus Solitarius**

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Binge eating disorder involves the consumption of larger amounts of food than normally would be eaten within a discrete period of time. The hormone glucagon-like peptide-1 (GLP-1) is produced peripherally by L-cells in the intestine and centrally in the nucleus tractus solitarius (NTS) of the hindbrain, and acts to suppress feeding and weight gain. GLP-1-producing preproglucagon (PPG) neurons in the NTS represent the major central source of GLP-1. Previous research has established the role of GLP-1 in motivation, reward, and feeding, but there is little known on its interaction with binge eating. Here, we tested the hypothesis that GLP-1 production in the NTS would be downregulated in rats with a history of binge-like palatable food intake. Male rats received access to fat (vegetable shortening) for 1h either every day (Daily, D) or only 3 d/week (Intermittent, INT) (n=7-8/group). Under these conditions, INT rats displayed increased fat intake compared to D rats (e.g., displayed binge-like eating). After 8 weeks of INT or D maintenance, rats were fasted overnight, and sacrificed at approximately the same time of day that fat access would have been given. Plasma and brains were collected to evaluate GLP-1. INT rats had a significant decrease in the expression of PPG mRNA in the NTS compared to D rats ($p < 0.05$). In contrast, plasma GLP-1 was significantly increased in the INT group versus D rats ($p < 0.05$). No significant differences were observed in NTS GLP-1 receptor expression, plasma insulin levels, or fasted blood glucose between groups. These results support the hypothesis that binge-like eating suppresses GLP-1 expression in the

NTS, and furthermore, demonstrate that a history of binge-like eating differentially impacts plasma versus central GLP-1 in rats.

P28 **Amylin&Rsquo;S Action On Cgrp And Dbh Neurons In The Lateral Parabrachial Nucleus**

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The lateral parabrachial nucleus (LPBN) consists of a complex of neurons in the dorsolateral pons and it plays an important role in a variety of visceral functions such as taste, respiration, central cardiovascular control and sleep. Previous studies in mice identified a group of neurons located in the LPBN that express calcitonin gene-related peptide (CGRP) and have an important role in appetite control. LPBN is a crucial brain site mediating the anorectic effect of amylin, a pancreatic hormone considered promising as pharmacotherapy for obesity. The aim of this study is to define the phenotype of amylin activated neurons in the LPBN. In particular, whether they are CGRPergic and noradrenergic, i.e. express the noradrenergic marker, dopamine beta hydroxylase (DBH). Thus, rats injected with either vehicle or amylin (50 ug/kg) were perfused 90 min later. Brains were then cut and stained for c-Fos-DBH and c-Fos-CGRP, resp., using immunohistofluorescence. Amylin activated c-Fos in the LPBN (P< 0,001) which was co-localised with CGRP and DBH positive fibers: »33% of specifically amylin-activated cells were DBH-positive (38 ±1 cells) and »38% were CGRP-positive (69 ±8 cells). Interestingly, amylin increased CGRP and DBH neuronal fibers by 4-fold and 3-fold respectively (P< 0,001).Indeed, in triplestaining for c-Fos-DBH-CGRP, we observed that amylin activated CGRP neurons are also directly innervated by noradrenergic neurons. By silencing CGRP activity in LPBN, using gene transfer vectors based on adeno-associated virus (AAV) and by inhibiting CGRP neurons in *Calca*^{Cre} mice (the Calca gene codes for calcitonin and CGRP), we will now test whether the absence of CGRPergic LPBN neurons will attenuate amylin's ability to reduce food intake and to stimulate neuronal activity.

P29 **Gdf15-Induced Anorexia In Rats And Shrews Is Driven By Malaise**

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Growth differentiation factor-15 (GDF15) is a cytokine implicated in the central regulation of energy balance. An active area of investigation is the potential use of GDF15-based approaches for the treatment of energy-balance disorders, including obesity and anorexia. GDF15 increases are associated with cancer progression and severity, chemotherapy and morning sickness, leading us to hypothesize that the anorectic effects of GDF15 may be mediated by malaise. First, GDF15 was administered 4thICV in rats and food and kaolin consumption (i.e. pica, an established proxy for nausea/malaise) were measured over 24h. Further, to evaluate if GDF15 effects on feeding require central glucagon-like peptide-1 (GLP-1) or/and serotonin signaling, rats were pre-treated with the GLP-1 receptor antagonist Exendin-9 (Ex-9) or the antiemetic 5-HT3 receptor antagonist Ondansetron (Ond). In addition, we tested the emetogenic and anorectic properties of GDF15 in the musk shrew (*Suncus murinus*), a mammalian model capable of emesis. GDF15 delivered 4thICV (30pmol) induced pica and anorexia in rats. Interestingly, the GDF15-induced malaise preceded the onset of anorexia. The observed behavioral responses seem to be independent of serotonin and hindbrain GLP-1 signaling as GDF15 effects were not prevented by either Ond (1mg/kg IP and 25ug 4thICV; respectively) or Ex-9 (10ug 4thICV). Furthermore, the highest dose of GDF15 tested (1mg/kg, IP) induced a strong emetic response in shrews at doses that only produced minimal suppressive effects on food intake and weight loss. Together our results suggest that GDF15 triggers anorexia by inducing nausea and emesis. Further studies are required to fully decipher the neuronal mechanisms engaged by GDF15 as well its application as a treatment for obesity.

P30 **Roux-En-Y Gastric Bypass Surgery Reprograms Enterocyte Triglyceride Metabolism And Postprandial Secretion In Rats**

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Roux-en-Y gastric bypass (RYGB) surgery produces rapid and persistent reductions in plasma triglyceride (TG) levels associated with fewer cardiovascular events. The mechanisms of the reduction in systemic TG levels remain unclear. We hypothesized that RYGB reduces intestinal TG secretion via altered enterocyte lipid handling. RYGB or Sham surgery was performed in diet-induced obese, insulin-resistant male Sprague-Dawley rats. First, we tested whether RYGB reduced test meal-induced TG levels in the intestinal lymph, a direct readout of enterocyte lipid secretion. Second, we examined whether RYGB modified TG enterocyte secretion at the

single lipid level and in comparison to other lipid subclasses, applying mass spectrometry lipidomics to the intestinal lymph of RYGB and Sham rats (0 to 21 days after surgery). Third, we explored whether RYGB modulated the metabolic characteristics of primary enterocytes using transcriptional and functional assays relevant to TG absorption, reesterification, storage in lipid droplets, and oxidation. RYGB reduced overall postprandial TG concentrations compared to Sham surgery in plasma and intestinal lymph similarly. RYGB reduced lymphatic TG concentrations more than other lipid subclasses, and shifted the remaining TG pool towards long-chain, unsaturated species. In enterocytes of fasted RYGB rats, lipid uptake was transcriptionally (*Fatp4, Fabp2, Cd36)* and functionally reduced compared to Sham, whereas TG reesterification genes were upregulated. Our results show that RYGB substantially reduces intestinal TG secretion and modifies enterocyte lipid absorption and handling in rats. These changes likely contribute to the improvements in the plasma TG profile observed after RYGB in humans.

P31 **Virtual Snack Portions Created Before Bariatric Surgery Predict Weight Loss One Year After Surgery Through 3-Month Change In Portion Created**

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Roux-en-y gastric bypass (RYGB) and vertical sleeve gastrectomy (VSG) reduce energy intake and are leading effective treatments for obesity. Virtual portion creation tasks (VPCT) serve as proxies for energy intake and could therefore predict success of surgery via weight loss outcome. RYBG (n=14) and VSG (n=28) surgery candidates created virtual portions of 8 snacks (apples, grapes, donuts, milk chocolate, edamame, olives, pretzels and chips), crossed by taste (sweet, salty) and energy (high, low), that were the "most they could tolerate eating" (MAX). Additionally, participants indicated their liking (VAS) of each snack and how often they ate the snack (days/yr). These tasks were administered 1-2 wk before (BL) and 3 mon after (3M) surgery. There were no differences in baseline weight and weight loss at 12 mon between RYGB and VSG subgroups ($p>.05$), therefore patient data was pooled for analyses. MAX at BL of sweet, low energy snacks positively predicted weight loss at 12 mon through partial mediation of MAX portion difference (BL-3M) weight loss ($\beta=0.03$, SE: 0.01, $Z=2.62$, $p=0.008$) as did salty, high energy dense snacks ($\beta=0.05$, SE: 0.02, $Z=2.47$, $p=0.0137$). Sweet, low and salty, high energy dense snacks were the highest liked (68-79 on a 100mm VAS scale) and highest consumed (60-116 days/yr) snacks in this sample. VPCT for large portions of preferred snacks are predictive of intermediate weight loss after bariatric surgery and could be used in pre-surgical behavior intervention.

P32 **Weighing Inhibits Food Primes To Stimulate Consumption.**

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Frequent weighing has been found to prevent age-related weight gain and facilitate weight maintenance following diet-induced weight loss. Watching food commercials is thought to act as a food prime and to stimulate eating. The following study was performed to examine the hypothesis that one means by which frequent weighing may inhibit weight gain, or regain, is by blocking the effect of food primes to stimulate eating. A total of 137 participants were divided into four groups. Half the participants were shown three short videos showing people eating food, the other half were shown non-food videos. In a 2 x 2 design, half of the participants were weighed just before they entered the testing room while the other half were not weighed. All participants were asked to rate how compelling they felt the videos were. A small bowel of chocolates was placed before each of the participants and were asked to eat as much or as little as then desired during the session. The results indicated that those who were not weighed and watched the food videos consumed significantly more chocolate than those who watched the non-food videos. However, being weighed prior to testing significantly blocked the effect of the food primes (bowl of chocolate) to increase intake. The results support the hypothesis that act of weighing suppresses the action of food primes to stimulate intake.

P33 **Are Personalised Weight Control Primes More Effective For Reducing Women&Rsquo;S Snack Intake Compared To General Weight Control Primes?**

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Previous research has shown that cues associated with weight control (e.g. slim models, low calorie foods) can reduce food intake in individuals who hold strong weight control goals. According to the Goal Conflict Model of Eating Behavior (Stroebe et al. 2013), cues *most* associated with weight control constructs should be most effective for activating weight control goals and reducing food intake. This study examined the effect of self-selected (personalised) weight control cues on snack intake compared to general weight control and neutral-control cues. Women (n=18; *M*:42.0 ± 12.1 years) who were overweight or obese (*M*: 30.4 ± 4.0 kg/m^2) and indicated strong goals to lose weight were recruited. From six weight control-related images participants individually selected an image that they most (personalised) and least (general) associated with weight control

and education (neutral control). Using a within-subjects design, participants were provided with a fixed-caloric lunch and after 2.5 hours the effect of exposure to personalised, general and control cues on snack energy intake were assessed in the laboratory. ANCOVAs controlling for cognitive restraint and disinhibition showed that snack intake (kcal) did not differ between personalised (*M*: 398.6 ± 190.5 kcal), general (*M*: 399.6 ± 211.1 kcal) and neutral-control (*M*: 378.9 ± 205.9 kcal) conditions, p = ns. The study findings do not provide any support that personalised, self-selected weight control cues are more effective than general weight control cues for reducing snack intake in women with goals to lose weight. Further research is needed to explore which types of cues and under which conditions weight control cues reduce food intake in individuals with weight control goals.

P34 **Intermittent Fasting Reduces Pancreatic Fat And Prevents Type 2 Diabetes In Mice**

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Obesity is accompanied by ectopic fat deposition in peripheral tissues including liver, muscle, and pancreas, but the impact of pancreas fat on islet cell biology and type 2 diabetes (T2D) risk is still poorly understood. Intermittent fasting (IF) is known to improve glucose homeostasis and insulin sensitivity in mice and humans. Under a high-fat diet, male New Zealand Obese (NZO) mice develop obesity as well as T2D, whereas obese B6.V-ob/ob (ob/ob) mice are diabetes-resistant. We aim to investigate whether IF affects pancreatic fat cell accumulation in diabetes-prone NZO mice and whether pancreatic adipocytes directly influence islet cell function. We fed NZO mice either a high-fat diet *ad libitum* or fasted them every other day and ectopic fat accumulation, glucose homoeostasis, insulin sensitivity, and islet function was analyzed and compared to results obtained from *ad libitum*-fed ob/ob mice. To study the direct effect of pancreatic adipocytes on islet glucose-stimulated insulin secretion, co-culture experiments were performed. Diabetes-resistant ob/ob mice displayed higher liver fat (~4-fold) but lower pancreatic fat (-46%) as compared with diabetes-prone NZO mice. IF in NZO mice resulted in lower pancreatic fat (-32%) as well as in improved glucose tolerance, insulin sensitivity, and islet function. Co-culture experiments demonstrated that pancreatic adipocytes induce insulin hypersecretion in mouse islets. Our data indicate that pancreatic adipocytes participate in the development of islet dysfunction and T2D in NZO mice and that IF represents an efficient strategy to decrease pancreatic fat deposition and T2D risk.

P35 **Obesity Following High-Fat Diet Ingestion And Subsequent Weight Loss - Searching For Epigenetic Mechanisms / Markers**

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The hypothalamic arcuate nucleus (ARC) plays an important role in body weight regulation by a balance between anorexigenic (POMC, CART) and orexigenic (NPY, AgRP) neuropeptides. The cleaved product of POMC, αMSH, is secreted and binds to receptors such as the Melanocortin 4 receptor (Mc4r) in the hypothalamic paraventricular nucleus (PVN). Its binding transmits a signal of hunger/satiety. Our goal is to investigate whether obesity caused by consuming a diet rich in calories and fat can be reversed by caloric restriction and what are the epigenetic mechanisms governing this process. Both high fat diet (HFD) and caloric restriction (CR) affected body weight in rats. HFD fed rats weighed more than chow fed rats, and caloric restriction from PND 90, reduced the rat's body weight. In parallel, Mc4R mRNA expression levels were highest in the chow group while in the CR group it remained similar to that of the HFD group. Since we identified a long-term effect of HFD on gene expression we hypothesized that it is due to epigenetic regulation. Indeed, the HFD and chow groups showed a similar methylation profile at the Mc4r coding region while dieting either by caloric restriction (on chow) or even by free feeding with chow resulted in higher methylation levels. Additionally, we found differences in histone modification at the same location. A potential effector of Mc4r which binds to the aforementioned segment of its DNA is CREB. Examination of its binding levels showed negative correlation with methylation levels and positive correlation with Mc4r expression levels. We suggest that the epigenetic alterations after dietary change are a mechanism the body uses in order to restore its formerly acquired weight set point.

P36 **Evaluation Of Methods For Measuring Food Reward And Food-Related Behavior In Healthy Individuals &Ndash; The Preset Study**

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Most of our daily decisions and actions affecting our energy balance are driven by implicit and explicit motivational processes. In an obesogenic environment where highly palatable and energy-dense foods are easily available, it is of great interest to increase our understanding of both implicit and explicit processes of food-related behavior by developing more extensive methods to measure these. The **objectives** of this study were to examine whether biometric signatures in response to visual food stimuli during the Leeds Food Preference Questionnaire (LFPQ) correlate with liking, wanting, food choice, or subsequent *ad libitum* food intake of those foods as assessed by the LFPQ and a taste task. This study explores food-related behavior by combining existing **methods** for measuring food reward with physiological, emotional and attentional aspects of food processing in 100 women and men with BMI ≥18.5 and < 25. During a computerized questionnaire we measure components of food reward using the LFPQ in combination with measures of autonomic nervous system activity using galvanic skin response, emotional response using facial expression analyses, and visual attention using eye tracking. Measurements are conducted during visual stimuli of food images varying in fat content and sweet taste, and results from measurements are related to actual food intake and food choice during an *ad libitum* taste task. Data collection is ongoing and preliminary results from the study will be presented at the conference in July. The study evaluates novel methods that can be used in future intervention studies to measure changes in food reward and food-related behavior.

P37 **Unraveling Mechanisms Underlying Release Of Neuropeptides From Neuronal Dendrites Using Novel Cell Biosensors**

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Dendrites are now recognized to be active transmitting neuronal compartments subserving complex brain functions, including motor behaviors and homeostatic neurohumoral responses, among others. Still, the precise mechanisms underlying activity-dependent release of dendritic signals, and how dendritic release can be regulated independently from axonal release of signals, remain largely unknown. We developed “sniffer” biosensor cells to enable the measurement and study of activity-dependent dendritic release of vasopressin (VP) from hypothalamic neurons. Dendritic release of VP was strengthened by clustered firing, compared to continuous irregular activity. Moreover, release evoked at any given frequency was robustly potentiated when firing was triggered by NMDA receptor (NMDAR) activation. Differently from axonal release, NMDAR activation was necessary for dendritic release to occur at physiological firing frequencies, acting thus as a potential gating mechanism by which activity-dependent release from these two neuronal compartments could be differentially regulated. The NMDAR-mediated potentiation of dendritic release was independent of a particular action potential waveform or firing pattern evoked, but correlated with higher dendritic Ca^{2+}levels. Overall, our studies provide fundamental novel information regarding stimulus-secretion coupling at neuronal dendrites.

P38 **A Neural Circuit Mechanism For Monitoring And Controlling Ingestion**

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The brain monitors negative sensory feedback from the digestive tract to limit excessive food and water intake, but the underlying neural substrate remains unclear. Here we show that a specific subpopulation of neurons in the parabrachial nucleus monitor the intake of both fluids and solids, using mechanosensory signals transmitted from the stomach. Activation of these neurons is avoided, and produces sustained appetite-suppressing signals to discourage the initiation of feeding and drinking. In contrast, inhibiting this population induces overconsumption only if a drive for ingestion exists, confirming that these neurons mediate negative feedback signaling. These findings provide a neural mechanism underlying mechanosensory monitoring of ingestion and negative feedback control of intake behaviors upon aversive gastric distension.

P39 **Hyper-Palatable Foods: Application Of A New Quantitative Definition To The United States Food Database**

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Background: Hyper-palatable foods (HPF) are comprised of combinations of sugar, fat, sodium, and/or carbohydrates and can facilitate overeating by circumventing satiety mechanisms. HPF are defined in the human literature using descriptive terms (e.g., fast foods, sweets), and there is no standard definition of HPF. A quantitative definition of HPF would facilitate greater specificity in identifying HPF and allow for better characterization of prevalence within the United States food system. The study purpose was to derive a quantitative definition of HPF and apply the definition to the 2016 US Department of Agriculture (USDA) Food and Nutrient Database, which contains most foods available in the US food system. Methods: Descriptive HPF definitions from the literature were entered into nutrition software to obtain numeric data on ingredients. We used a data-driven approach to derive the composition of HPF, with a focus on percent calories from fat, simple sugars, and complex carbohydrates, and percent sodium/food weight. These criteria were then applied to the USDA database to determine the prevalence of HPF. Results: Hyper-palatable items comprised 37% (2908/7849) of foods in the US food system. Almost half (42%; 1232/2908) of HPF items were processed/cooked meats and meat-based dishes high in fat and sodium. Grains (e.g., breads, salty snacks) comprised 19% of HPF items (563/2908). Vegetables cooked in fat, sodium, and/or sauces accounted for 14% of HPF (418/2908). Items labeled as low/reduced fat/sugar/salt/calories comprised 5% of HPF (159/2908). Conclusion: Using a data-

derived definition of HPF, findings revealed a substantial percentage of foods in the US food system may be hyper-palatable, including foods not previously conceptualized as hyper-palatable.

P40 ***Digestion-Ready:* A New Term To Replace *Hunger***

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Research into hunger is beset by terminological imprecision. Janowitz advocates *hunger* and *appetite* be banished for "the sake of linguistic peace." Mattes and Friedman muse that uses of the word hunger seem as varied as the food used to satisfy it. *Hunger* is frequently conflated with *appetite* (the desire to eat) not only in lay parlance but in the academic literature. Furthermore *what it is like* to experience physical hunger, the hunger pang, or Empty Hollow Sensation (EHS), is commonly unrecognised or ignored. For many, *what it is like to be hungry* turns out to be anxiety, sadness, pain, nausea, fatigue or thirst. A host of non-specific somatic sensations thus get reported as hunger when subjects complete hunger scales. *What is it like to be digestion-ready?* One feels an empty hollow sensation just below the rib cage. *Is digestion-ready just the EHS?* The EHS is a necessary condition for digestion-readiness. I am with Walter Cannon who described the hunger pang as*: …an exhibition in the digestive organs of readiness for prompt attack on the food*.. Other contributory conditions to digestion-readiness include sitting to eat, in a calm state of mind and not late at night. *Can digestion-readiness be measured?* Epigastric sensations of emptiness have been associated with phase III contractions of the migrating motor complex. These contractions are a preparation in the bowel for food intake, and are thus an objective marker of readiness to digest. *Is digestion-readiness a good thing?* The EHS has been correlated with weight loss, improved insulin sensitivity and reduction of H. Pylori antibodies. Clarity of terminology is essential for testable theory. I suggest the term digestion-ready as a conceptual tool to help relieve a scene of theoretical confusion.

P41 **The Different Genetic Architectures For Overweight In Tall Versus Short People**

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Obesity is more common in short people than in tall people. Body mass index (BMI) is one of the most common measures to index obesity [1]. Although BMI attempted to correct height in the calculation by dividing square of height, the significant negative association between BMI and height still exist (beta=-0.036, p< 2E-16 for male, beta=-0.106, p < 2E-16 for female) in our study. Both genetic and environmental factors contribute to the variation in obesity between short and tall people as they differ in growth hormone level (negatively associated with the amount of ectopic fat deposition) [2], energy consumptions, lean mass, fixed portion size and baseline metabolite rates. Moreover, a deficit in the gravitostat (an unknown signal from bone that reduces appetite and increases upon weight loading), is likely to impact more on obesity in tall people [3]. Therefore, height may be a confounding factor when analyzing the genetic architecture of BMI. The Genome-wide association study (GWAS) of BMI have elucidated the genetic architecture of obesity [4]. However, Identifying the genes that cause obesity in tall versus short people, which has not been studied, maybe key towards unraveling novel pathways to induce obesity. Hence, we performed a range of genetic analyses on existing whole genome data to disentangle height-dependent differences in genetic determinants of BMI. Firstly, we compressively investigated BMI profile in UKbiobank cohort (n=492,580) in different population hierarchies (age, sex and height). In addition, we conducted height -adjusted BMI GWAS and GWASs of BMI in height stratified subpopulations to identify the genetic variants which are not confounding with height and height-specific genetic variants associated with BMI.

P42 **Inhibitory Control Training For Binge-Subtype Eating Disorders: A Feasibility And Acceptability Study Using Top-Down And Bottom-Up Approaches**

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Background: In response to the limited effectiveness of current evidence-based treatments for bulimia nervosa and binge eating disorder, the current study aimed to examine the feasibility and acceptability of combining techniques to target top-down (implementation intentions) and bottom-up (inhibitory control training) processes. The primary outcomes measured were binge-eating frequency and high calorie food valuation within binge-subtype eating disorder samples. **Method:** Using a combined between / within subject design, seventy-eight participants with bulimia nervosa and binge eating disorder were allocated to one of two inhibitory control intervention groups (food-specific versus general) for four weeks. **Results:** Although engagement with the intervention was sub-optimal, both intervention groups achieved significant reductions in binge eating frequency and high calorie food valuation at post-intervention. The difference between food-specific and general inhibitory control training was not significant, but the effect size reduction in primary outcomes was greater for the food-specific intervention group. **Conclusion:** Food-specific inhibitory control training for binge-subtype eating disorders may be a useful method of reducing binge-eating frequency and high-calorie food valuation. Limitations, clinical implications, and recommendations for future research are discussed.

P43 **Personality Moderates The Effectiveness Of A Novel Healthy Eating Mobile App.**

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Reduced self-control is a strong predictor of overeating and obesity. Priming a self-control mind-set has been shown to reduce snack consumption in the lab in the presence of a cue reminder. However the long-term and real-world effects are not known. The use of digital technology is an efficient way to deliver self-control cues in real-world settings. Many mobile apps claim to support healthy eating but few are grounded in psychological theories of self-control. The aim of this study was to develop and test the feasibility and effectiveness of a novel, evidence-based mobile app to promote healthier eating. Furthermore, the mediating and moderating influences of key personality traits were examined. Using an iterative process involving users at every stage of the process, a prototype mobile app was developed. The final version included a self-control priming task, sent personalised reminder cues before each eating occasion and provided a just-in time 'crave buster' for unanticipated eating opportunities. In a longitudinal trial the app was then used over an eight-week period (N=71) with pre-post measures of weight, per cent body fat and food intake. The app received high usability ratings on the Suschapt Usability Scale (M=76.55; SD=11.35), however food intake, per cent body fat and weight pre- and post- app use showed no significant differences ($p>.05$). Exploratory analyses showed that app effectiveness ratings and weight loss were moderated by several key personality traits. These findings indicate that the app was user-friendly but only effective for individuals with certain personality types. Future app development in this area should consider the personality of the user for optimal support and effectiveness.

Friday, July 12, 2019

8:30 - 10:30 AM	Progress
SYMPOSIUM 5: Counteracting Desire in the Obesogenic Environment	

Chair(s): Ciaran Forde and Laurence Nolan

8:30 **From Extinction Science To Exposure Interventions To Reduce Eating Desires**
ANITA JANSEN, GHISLAINE SCHYNS, ANNE ROEFS
Maastricht University, Maastricht, Netherlands

"Eat less, eat better, exercise more: change your lifestyle". This is the advice overweight people usually get. However, most of the obese people do know this and if they could change their lifestyle, obesity was not a problem. It appears to be extremely difficult to change one's lifestyle and eating habits. Learned appetitive responding, or food cue reactivity, is a strong motivator to eat, even in the absence of hunger. Cued desires and cued cravings might sabotage healthy eating, induce weight gain and impede weight loss or weight loss maintenance. Then, the extinction of appetitive responding could be helpful to eat less and lose weight. In this presentation, the science of desire extinction is discussed and the translation to exposure treatments for overeating is made.

9:00 **Targeting Reward And Inhibition To Decrease Overeating**
KERRI N. BOUTELLE
UC SAN DIEGO, LA JOLLA, CA, United States

Food is an unavoidable, motivationally salient cue. The influence of the current food environment, coupled with the inherent trait to overeat when exposed to food cues, has led to weight gain in vulnerable individuals. Binge eating and overeating can be conceptualized as a balance between the drive resulting from the rewarding aspects of food and an individual's ability to inhibit those urges. We have developed a treatment program, called Regulation of Cues (ROC), which specifically targets two mechanisms; decreasing external food cue responsivity (reward) and improving appetite sensitivity (inhibition). Our data with children and adults suggests that the ROC program is promising for decreasing binge eating, overeating, and weight. This presentation will review the research supporting the role of these two mechanisms in overeating and binge eating, as well as our efforts to address these mechanisms. By targeting underlying mechanisms, we may be able to improve treatments for overeating and weight loss.

9:30 **Social Inequality As An Obesogenic Environment: Implications For Socioeconomic Disparities In Obesity**
BOBBY K. CHEON[1, 2]
[1]School of Social Sciences (Psychology), Nanyang Technological University, Singapore, Singapore, [2]Clinical Nutrition Research Centre, Singapore Institute for Clinical Sciences, A*STAR, Singapore, Singapore

Prior research has revealed socioeconomic disparities in obesity with poorer individuals at greater risk. Yet studies on interventions that seek to alleviate food insecurity and economic/structural barriers to healthier diets among the poor have produced mixed results, suggesting other aspects of the experience of poverty may be contributing to preferences and eating behaviors linked to obesity. In this presentation, I propose that perceptions of social inequality and disadvantage compared to others are sufficient to promote increased energy intake independent of poverty. Across numerous studies, I will demonstrate how perceptions of socioeconomic inadequacy compared to others (in the absence of actual socioeconomic deprivation) may systematically alter one's relationship with food across multiple levels of analysis (attitudinal, behavioral, perceptual and physiological). Specifically, experimentally-induced feelings of having lower socioeconomic status compared to others increases subsequent preferences for energy-dense foods, greater energy intake from snacks and meals, increased circulation of ghrelin, blunted feelings of fullness following isocaloric food consumption, and heightened taste-based perceptual sensitivity to the presence of energy in foods. Notably, these effects were largely unrelated to stress or negative emotions. Finally, I will discuss results from a 2-week intervention to alleviate perceptions of deprivation and disadvantage compared to others on portion selection and dietary patterns. Together these studies critically reveal that perceived social inequality may have inherently obesogenic properties that could contribute to excess energy intake independent of the financial/structural constraints produced by poverty itself.

10:00 **Regulation Of Craving: From Neural Mechanisms To Treatment Development**
HEDY KOBER
Yale University, New Haven, CT, United States

In this invited talk, I will first describe one important aspect of the obesogenic food environment: food cues that lead to craving. In this context, I will present a quantitative meta-analysis that demonstrates that cue exposure, cue reactivity, and cue-induced craving prospectively predict eating as well as weight gain over time, consistent

with a causal role (Boswell & Kober, 2016). I will then describe the Regulation of Craving (ROC) task, and its application in several lines of work including: (i) as a tool to experimentally assess the efficacy of regulation strategies to modulate cue-induced craving (e.g., strategies drawn from cognitive-behavioral treatments; CBTs); (ii) as a tool to investigate the basic neural mechanisms underlying craving and its regulation; and (iii) as the basis for novel mechanism-focused interventions that improve food choices and reduce caloric consumption – and might inoculate individuals against the obesogenic food environment. Along the way, I will argue that CBT-based regulation of craving depends on recruitment of dorsolateral and ventrolateral prefrontal cortex, and that – unlike CBT – mindfulness-based treatments may lead to reduced "bottom-up" reactivity during craving (as well as other emotions). I will also discuss behavioral and neural similarities between food and drug craving, as well as my broader approach to uncovering the neural mechanisms that may underlie treatment-related change, including improvement in food choices.

8:30 - 10:30 AM	Mission 1
ORAL SESSION 5: Nutrient Effects on Brain	

Chair(s): Clemence Blouet and James McCutcheon

8:30 **Nutrients And Drugs Of Abuse Modulate Hypothalamic Neuron Activity Via Distinct Pathways**

AMBER L ALHADEFF, NITSAN GOLDSTEIN, J NICHOLAS BETLEY
University of Pennsylvania, Philadelphia, PA, United States

How does the brain process natural versus drug rewards? While midbrain dopamine circuits are activated by both types of rewards, if and how drugs of abuse affect classic homeostatic feeding circuits remain largely unknown. We assessed the neural activity dynamics of hypothalamic agouti-related protein (AgRP)- and pro-opiomelanocortin (POMC)-expressing neurons during administration of caloric (e.g. alcohol) and non-caloric (e.g. cocaine, nicotine, etc.) drugs by monitoring *in vivo* calcium dynamics with fiber photometry. We unexpectedly found that, unlike nutrients, drugs of abuse inhibit neural activity in *both* AgRP and POMC neurons, suggesting that drugs signal hypothalamic neurons through a pathway distinct from calories. In support of this notion, alcohol does not condition sensory cues to affect hypothalamic neuron activity, unlike other macronutrients. Furthermore, AgRP neuron stimulation resulted in robust glucose, but not alcohol, intake. Given these differences, we sought to define the pathways through which natural and drug rewards signal hypothalamic neurons from the periphery. To do so, we monitored AgRP neuron activity during gastric infusion of nutrients or alcohol in mice with a complete subdiaphragmatic vagotomy. Strikingly, alcohol maintained the ability to modulate hypothalamic neurons in the absence of vagal gut-brain signaling, unlike fat and gut-released satiation signals. Taken together, these data demonstrate that nutrients and drugs of abuse can engage at least two pathways (vagal and non-vagal) to modulate hypothalamic neuron activity.

8:45 **Fats And Sugars Recruit Distinct Peripheral Neural Circuits To The Brain**

MOLLY J. MCDOUGLE, ALAN M. DE ARAUJO, ARASHDEEP SINGH, GUILLAUME DE LARTIGUE
University of Florida, College of Pharmacy, Department of Pharmacodynamics, Gainesville, FL, United States

Nodose ganglia (NG) neurons transmit metabolic information from the gut to the brain. It remains unclear whether macronutrients signal through different vagal circuits. **Methods**: We employed a novel Fos^{CreER} mouse line crossed with $tdTomato^{Flox}$ mice to genetically label neurons that were activated by defined gut metabolic stimuli. Saline (500ul), sucrose (75%), or equicaloric lipid (33%) were infused through implanted gastric catheter and 4-hydroxytamoxifen (30mg/kg i.p.) given to permanently trap fluorescence in activated neurons. After 2 weeks, mice received gastric infusion of the same or different solution (n=5/group). Brain, NG, small intestine, and hepatic portal vein (HPV) were collected 90 minutes later. Nucleus tractus solitarius (NTS) was sliced and stained for cFos. Colocalization with tdTomato was quantified. NG was imaged for tdTomato+ cells, and peripheral tissues were analyzed for tdTomato+ vagal fibers. **Results:** tdTomato expression was low in the NTS and absent in NG neurons following saline infusion, but increased after either sucrose or fat ($p< 0.05$). There was extensive (65.2%) overlap of cFos+ and tdTomato+ neurons in the NTS when the same stimulus was given at both timepoints. Colocalization was reduced in mice that received sucrose infusion followed by lipid (25.8%). Crucially, tdTomato+ fibers were observed in the HPV of sucrose-treated mice, and to a much lower degree in lipid-treated mice, while absent in saline controls. Conversely, lipid-treated mice had higher levels of tdTomato+ fibers in the duodenum and jejunum, compared to both sucrose- and saline- treated mice. **Conclusion:** We used a genetic approach to deconstruct the NG and NTS into cellular components and identify distinct neuronal pathways signaling lipids vs. sucrose from the gut.

9:00 **Striatal Activity Decreases Following The Intragastric Infusion Of Glucose And Lipids In Lean Humans**

KATY A. VAN GALEN[1], KASPER W. TER HORST[1], ANOUK G. SCHRANTEE[2], SUSANNE E. LA FLEUR[1,3], JAN BOOIJ[4], MIREILLE J. SERLIE[1]
[1]Department of Endocrinology and Metabolism, Amsterdam UMC, location AMC, Amsterdam, Netherlands, [2]Department of Radiology, Amsterdam UMC, location AMC, Amsterdam, Netherlands, [3]Department of Clinical Chemistry, Amsterdam UMC, location AMC, Amsterdam, Netherlands, [4]Department of Nuclear Medicine, Amsterdam UMC, location AMC, Amsterdam, Netherlands

Striatal dopamine signaling is involved in reward and the motivation to eat. Animal studies showed that nutritional signals that arise following the ingestion of nutrients induce striatal dopamine release. These post-ingestion nutritional signals may therefore play an important role in the rewarding aspects of food consumption and the regulation of feeding behavior. To study this in humans, we assessed the taste- and preference-independent effects of glucose and lipids on striatal activity in lean humans. In 15 lean humans, we assessed the effects of direct intragastric infusions of glucose 50% (250ml, 500kcal), Intralipid ® (250ml, 500kcal) and water (250ml) on the BOLD signal of striatal subregions (the nucleus accumbens, the caudate nucleus and the putamen), using functional MRI. Relative to the infusion of water, intragastric glucose infusion induced a significant decrease in BOLD signal in the nucleus accumbens ($p< 0.001$), caudate nucleus ($p=0.049$) and putamen ($p=0.006$). The intragastric Intralipid® infusion induced a significant decrease in the nucleus accumbens ($p=0.025$) and putamen ($p=0.025$). There was no difference between the effects of glucose and Intralipid® infusion on neuronal activity in these striatal regions. These findings show that, in lean individuals, striatal neuronal acitivity is reduced following the intragastric infusion of macronutrients in a taste- and preference independent manner. These data suggest an important role for post-ingestion nutritional signals in the

regulation of hedonic eating behavior. We are currently assessing these post-ingestion nutritional effects in obese individuals before and after weight loss.

9:15 **Effects Of 8-Week High Fat Diet On Brain, Behavior, And Perception In Healthy Humans**

ALEXANDRA G DIFELICEANTONIO[1,2,3], SHARMILI EDWIN THANARAJAH[3,4], KERSTIN ALBUS[5], OLIVER CORNLEY[5], JENS C BRUENING[3], MARC TITTGEMEYER[1,3], DANA M SMALL[1,2]

[1]Modern Diet and Physiology Research Center, New Haven, CT, United States, [2]Department of Psychiatry, Yale University, New Haven, CT, United States, [3]Max Planck Institute for Metabolism Research, Cologne, Germany, [4]Department of Neurology, University Hospital of Cologne, Cologne, Germany, [5]Cluster of Excellence Cluster at the Univeristy of Cologne, Cologne, Germany

There is clear causal evidence from animal studies that a high fat diet can alter dopamine signaling and impair dopamine-dependent functions. Emerging work in humans also supports a causal relationship; though few studies collect comprehensive measures of diet, metabolism, and adiposity, which may all contribute to brain alterations. Here, we collected perceptual, metabolic, neural, and behavioral measures before and after 49 healthy-weight participants were assigned to consume either a high protein yogurt (~50% kcal from protein) or an equicaloric high fat (~40% kcal from fat) yogurt twice daily for 8-weeks. Despite no change in adiposity or metabolic measures, diet influenced fat preference and brain response to a high fat/high sugar milkshake. More specifically, participants in the high-fat, but not the protein intervention reported lower desire to eat the low fat pudding. Paralleling the behavioral finding, response to milkshake in the caudate nucleus (p=0.029, FWE small volume) and vmPFC (p=0.049, whole brain FWE) was decreased after the high-fat, but not high-protein intervention (group*time). In the insula, brain response to milkshake was increased in the high-fat compared to the high-protein group (bilateral, p=0.009 and p=0.024 whole brain FWE). These data support a causal influence of high-fat diet on fat preference and on neural circuits responding to palatable foods independent of adiposity or metabolic health.

9:30 **Exclusively Drinking Sucrose Early In Life Alters Adult Drinking Behavior**

K. LINNEA VOLCKO[1,2], JOHN T. PRZYBYSZ[1], DESTINY J. BRAKEY[1,2], DEREK DANIELS[1,2]

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

Proper fluid balance is critical for life. Severe dehydration is deadly and modest dehydration can have deleterious consequences on physiology and cognitive function. Learning plays an important role in shaping the appetitive behaviors required for drinking. Children often forego drinking plain water and instead consume beverages such as milk and juice. What effect this may have on adult behavior remains an open question. To model aspects of the human condition, we bred Sprague-Dawley rats in a cage that prevented the pups from obtaining fluid other than from nursing. Pups were weaned onto either tap water or a 5% sucrose solution, and given access to only that fluid for the next 8 weeks. We then measured intake of water or sucrose after (a) a mild hypertonic saline (HS) injection, and (b) overnight fluid deprivation. We also performed subsequent sucrose preference (two-bottle) tests after HS injection, then maintained all rats on water for one week and repeated the test. We found that rats maintained on sucrose drank less water than did rats maintained on water after a mild HS injection. After overnight fluid deprivation, rats maintained on sucrose drank less water and more sucrose in the first 10 min of the test, but intake by the end of the test was not different between the groups of rats. Although we observed a comparable number of licks across the whole test, microstructural differences in licking patterns were detected. Rats maintained on sucrose showed a stronger preference for sucrose, but group differences in preference were ameliorated after a week of drinking only water; however, differences in lick patterns for sucrose remained. These data provide evidence that adult drinking behavior is influenced by exclusively drinking sucrose early in life.

9:45 **Ability To Estimate Caloric Load And Expected Satiation Varies By Macronutrient Content**

SOPHIE P. FROMM[1], ARSENE KANYAMIBWA[1], ALEXANDRA G. DIFELICEANTONIO[1,2], KATHRYN M. WALL[1], KYLE FLACK[3], BARRY GREEN[4,5], DANA M. SMALL[1,6]

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Recent reports suggest that the ability to accurately estimate energy density of food depicted in images is poor, but may vary by macronutrient, with food containing fat being easier to estimate than food containing carbohydrate or carbohydrate and fat. We sought to replicate this finding with a novel picture set. We also aimed to test if actual energy density is associated with ratings of expected satiety, which may be easier to estimate than energy density. 61 healthy adults rated 60 images of ~120kcal food portions. 36 images were selected that were evenly divided into three categories: high in carbohydrate and low in fat (Carb), high in fat but low in carbohydrate (Fat) or high in fat and carbohydrate (Combo). Categories were matched on ratings of energy density, liking, familiarity, frequency of consumption, perceived healthiness and low-level visual input. As predicted, expected satiety was associated with actual energy density but the direction of association varied

between categories ($F(2,180)=13.809$, $p\leq.0001$), with a positive correlation for Fat and negative correlations for Carb and Combo. A parallel pattern was observed for the difference of associations between estimated caloric load and actual energy density ($F(2,180) = 13.88$, $p\leq.0001$), with a positive association for Fat and negative associations for Carb and Combo. Interestingly caloric load was overestimated for all categories with the greatest discrepancy for Combo foods (M=18.6 kcal, SD=19.03 for Combo, M=14.27, SD=23.66 for Carb, M=10.68, SD=20.23 for Fat). Our findings align with prior work in highlighting limited ability to estimate energy and satiety from carbohydrate or fat plus carbohydrate foods.

10:00 **Restriction Of Dietary Protein Leads To Rapid And Selective Preference For Protein And Elevated Neural Activity In Ventral Tegmental Area**

GIULIA CHIACCHIERINI[1], FABIEN NANEIX[1], KATE Z. PETERS[1], EELKE M. S. SNOEREN[2], JAMES E. MCCUTCHEON[1]

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Adequate intake of amino acids is essential for health and survival. Accordingly, tight regulation of dietary protein intake is seen in many species. However, there is still little understanding of how the brain encodes internal state related to protein restriction and how this affects motivation for food. We showed that protein-restricted rats (5% protein diet), compared to non-restricted rats (14% protein), developed a conditioned preference for a protein-rich solution (4% casein), relative to carbohydrate solution (4% maltodextrin). Expression of the calcium indicator, GCaMP6s, in the ventral tegmental area (VTA) allowed neural activity to be measured by photometry during drinking behaviour. In protein-restricted rats only, neural activity was greater when consuming protein than carbohydrate. Ongoing experiments are assessing dopamine release through expression of the dopamine sensor, dLight1.2, in the nucleus accumbens.Next, we investigated temporal dynamics of protein preference in a separate cohort and observed that protein preference developed within 3 minutes of the first exposure to nutrient-rich solutions.In addition, we examined whether motivation for food was altered by protein restriction using progressive ratio responding and found that, for nutritionally complete food pellets, there was no difference in breakpoint between protein-restricted and non-restricted rats. In summary, we showed that protein-restricted rats exhibited a strong protein preference that developed rapidly with minimal experience. Moreover, VTA activity reflected protein content of food when rats were protein-restricted. Finally, general motivation for food was not affected by protein-restriction, suggesting that protein restriction induces a selective protein appetite.

10:15 **Intermittent High-Fat Diet Intake Reduces Responsiveness To Intragastric Nutrient Infusion And Exogenous Amylin**

CALYN B. MASKE, ISABEL I. COIDURAS, ZELEEN E. ONDRIEZEK, DIANA L. WILLIAMS
Department of Psychology & Program in Neuroscience, Florida State University, Tallahassee, FL, United States

Intermittent (INT) access to high-fat diet (HFD) induces binge-like eating in rats. During INT HFD, we found that female rats consume more kcal than chow-maintained controls (2 h:45%; 20 h:21%), increasing meal size (169%)($P's< 0.05$). We hypothesized that impaired satiation contributes to this effect. To address this, female rats with intragastric (IG) catheters (n=6-9/group) received either chow, INT (20 h every 7^{th} day at dark onset) or continuous (CONT) access to 45% HFD in addition to chow. On test days, IG infusions (3.3 ml; 1 ml/min) of saline or Ensure Plus (5 kcal) occurred 15 min before dark, and food intake was measured continuously. Ensure reduced intake relative to saline in chow rats from 30 m (61%) to 10 h (13-21%)($P's< 0.05$). In CONT rats, Ensure reduced 30 m intake by 54% ($P< 0.05$). INT rats were tested on chow and INT HFD days. On each, the effect of Ensure emerged at 1 h and was of smaller magnitude (chow day:14%; HFD day:25%). Meal pattern analysis showed that the major effect of Ensure was on meal size, but this was not present in INT rats, suggesting a reduction in nutrient-induced satiation. In a second study, we tested the effect of amylin (5 or 10 μg/kg sc) using a similar design (n=13-18/group; INT HFD 20 h every 4^{th} day). In chow rats, both amylin doses lowered intake relative to vehicle from 30 m (47%) to 4 h (15%), and 10 ug/kg amylin reduced first meal size (32%)($P's< 0.05$). CONT rats showed a less robust response, only lowering intake after 10 μg/kg amylin (13-18%). On chow days, INT rats also failed to respond to 5 ug/kg amylin. During INT HFD access, amylin had no effect in INT rats. We conclude that impaired satiation responses, mediated in part by reduced sensitivity to amylin, may explain the elevated intake induced by INT HFD access.

10:30 - 11:00 AM	Transit Zone
Coffee Break	

11:00 - 12:00 PM	Progress
MARS LECTURE 3	

Chair(s): Suzanne Higgs

11:00 **Energy Expenditure Drives Energy Intake: Appetite Control Within An Energy Balance Framework**
JOHN E BLUNDELL
University of Leeds, Leeds, United Kingdom

Over 50 years ago Edholm, Widdowson and others hypothesised that the essence of appetite control could be found in the interactions between EE and EI. In the past 10 years several studies using this framework have found robust associations among body composition, RMR and EI. Since FFM and RMR were strongly associated with EI it was proposed that 'RMR represents the energy requirements of maintaining the functioning of the body's vital organs and constitutes a drive for energy; in other words the motivation to seek and eat food'. This makes sense from an evolutionary perspective. More recently an editorial in AJCN has echoed these findings and stated that 'RMR and FFM are the major determinants of EI'. This approach also raises the possibility that behavioural EE (Physical activity) and other forms of EE (eg BAT) constitute sources of the drive to eat. Evidence on these issues is accumulating, and shows that AEE can contribute to FM control through improving appetite by increasing E turnover. This approach together with hierarchical multiple regression has led to the proposal of separate roles for FFM and FM in the tonic control of appetite, and questions whether regulation is the correct term to describe operations within the energy balance system. This approach provides a 'molar' level of explanation which is transparent and plausible. This line of research gives a proximal description of the understanding human actions, and draws attention to the way in which biological, behavioural and psychological variables interact in the tonic and episodic expression of appetite. There are implications for understanding the development and management of obesity.

12:00 - 4:00 PM	Lunch On Own
LUNCH	

1:00 - 3:30 PM	Mission 1
Mock Study Section	

This session is intended to provide insight into the NIH grant review process for both new and experienced investigators. Dr. Raul Rojas, Scientific Review Officer for IPOD, will describe the study section process and will run a study section, Chaired by Dr. Tim Moran, in which three grants will be reviewed and scored. Subsequently Dr. Patrick Tso, will explain how grants are handled by council and Dr. Susan Yanovski, Program Director of Digestive Diseases and Nutrition at NIH, will summarize recent changes in requirements for grants that include human subjects. There will be an opportunity for questions regarding each stage of the review process.

Chair(s): Ruth Harris and Tim Moran

4:00 - 6:00 PM	Progress
SYMPOSIUM 6: Working Out the Benefits of Exercise	

Chair(s): John Blundell and Nu-Chu Liang

4:00 **Cellular And Synaptic Reorganization After Exercise Training**
KEVIN W WILLIAMS
The University of Texas Southwestern Medical Center, Dallas, TX, United States

Hypothalamic Pro-opiomelanocortin (*POMC*) and Neuropeptide Y/Agouti-Related Peptide (*NPY*/*AgRP*) neurons are critical nodes of a circuit within the brain that sense key metabolic cues as well as regulate feeding behavior, energy expenditure, and glucose metabolism. Importantly, intrinsic cellular properties of these neurons are highly sensitive to metabolic state. This includes a rapid reorganization of synaptic inputs and electrophysiological properties in order to facilitate adaptations to altered energy balance. While the cellular properties of these neurons have been investigated in the context of obesity, much less is known about the effects of exercise training. Here I will describe recent work from my lab investigating the effects of exercise on hypothalamic melanocortin neurons. We have shown that these neurons rapidly alter their activity in response to exercise, in a way that predicts changes in energy balance and glucose metabolism. Similarly, we have shown

that the effects of exercise (onset and duration) are temporally distinct in subsets of these neurons. I will discuss these findings and others on the plasticity of this circuit in response to exercise.

4:30 **Exercise Reverses High-Fat Diet-Induced Adaptions Of Perineuronal Nets Within The Prefrontal Cortex**

TRAVIS E BROWN[1], GEORGIA E KIRCKPATRICK[1], PAIGE M DINGESS[2], CARRIE R FERRARIO[3], BARBARA A SORG[4]

[1]University of Wyoming, Laramie, WY, United States, [2]University of Alaska, Anchorage, AK, United States, [3]University of Michigan, Ann Arbor, MI, United States, [4]Washington State University, Pullman, WA, United States

Previously, we reported that consumption of dietary high-fat resulted in adaptations to perineuronal nets (PNNs), structures surrounding fast-spiking parvalbumin (PV)-containing interneurons that critically regulate cellular function and plasticity within the prefrontal cortex (PFC). Specifically, we saw an attenuation in *Wisteria floribunda*lectin (WFA) staining, a marker for PNNs, within the prelimbic PFC and orbitofrontal cortex. However, whether the high-fat diet-induced adaptations to PNNs within the cortex can be reversed are unknown. I will discuss recent work within my laboratory that looks to address this question using an exercise regimen after 21 days of high-fat diet exposure. I will highlight data that exercise can reverse high-fat diet-induced changes in PNNs within the prelimbic mPFC but not the orbitofrontal cortex. In addition, I will show data that the same exercise protocol can reduce time-dependent increases in craving for foods high in fat (incubation of craving). Our findings suggest that there are region specific changes in PNNs within the cortex after exposure to dietary high-fat that may facilitate changes in the motivational circuits to promote maladaptive food seeking behaviors, which exercise may be able to reverse.

5:00 **Obesity, Dopamine, And Physical Activity**

ALEXXAI KRAVITZ
Washington University , St Louis, MO, United States

Obesity is associated with physical inactivity. Despite the importance of this relationship, the neural determinants of physical inactivity in obesity remain largely unknown. This lack of mechanistic understanding is paralleled by a lack of reliable methods for increasing physical activity levels in people with obesity. We believe an understanding of the cellular and molecular underpinnings of physical activity are needed to understand, and ultimately alter, the relationship between obesity and physical inactivity. To this end, we hypothesize that inactivity is caused by diet-induced alterations in dopamine function in people with obesity. Our hypothesis is based on two lines of evidence: 1) obesity has been linked to alterations in basal ganglia dopaminergic function in both humans and rodents 2) basal ganglia dopamine is both necessary and sufficient for altering movement levels in multiple species. To examine this hypothesis, we quantified the effects of high-fat diet on dopaminergic function, striatal neuronal firing, and physical activity in mice. We linked high-fat diet exposure to a deficit in striatal dopamine D2 receptors, and found that genetic removal of these same receptors was sufficient to decrease activity levels in lean mice. Identifying the biological determinants of physical inactivity may lead to better understanding of strategies for increasing physical activity, particularly in people with obesity.

5:30 **Relationships Between Physical Activity And White Matter Microstructure**

CLAIRE E SEXTON[1,2], ENIKO ZSOLDOS[2], MELIS ANATURK[2], NICOLA FILIPPINI[2], MIKA KIVIMAKI[3], ARCHANA SINGH-MANOUX[4], KLAUS P EBMEIER[2]

[1]University of California San Francisco, San Francisco, CA, United States, [2]University of Oxford, Oxford, United Kingdom, [3]University College London, London, United Kingdom, [4]INSERM, Villejuif, France

It has been hypothesised that physical activity (PA) has beneficial effects on white matter microstructure, and a meta-analysis of the animal literature reported that exercise is positively associated with myelin sheath thickness. However, the results of diffusion tensor imaging (DTI) studies examining PA in humans have been mixed. Part of this variance may stem from PA typically being measured at a single time-point. We examined the relationship between physical activity and white matter microstructure in 575 members of the Whitehall II Imaging Sub-Study (age 69.9 ±5.1 years, 19% female). DTI data was acquired at a single time-point (2012-2016) and processed using tract-based spatial statistics. PA was assessed using a modified version of the Minnesota leisure-time physical activity questionnaire at four previous time-points (1997-99, 2002-04, 2007-09, 2012-13) and MET.Minutes per week for moderate-to-vigorous PA (MVPA) calculated. Fractional anisotropy (FA), radial diffusivity (RD) and axial diffusivity (AxD) values were compared between active (≥ 500 MET.Minutes per week at ≥ 3 time-points) and inactive (≥ 500 MET.Minutes per week at < 3 time-points) groups using randomize. Age, gender and education level were included as covariates, and the significance threshold set at $p < 0.05$ using threshold-free cluster-enhancement. Overall, 204 participants were classified as inactive, and 371 as active. There were no significant differences between active and inactive participants in FA, AD or RD values. Latent growth class analysis of trajectories of PA over time may be more sensitive to differences in white matter.

4:00 - 6:00 PM	Mission 1
ORAL SESSION 6: Hot Topics in Ingestive Behavior	

Chair(s): Alexandra DiFeliceantonio and Carrie Ferrario

4:00 **Identifying Dissociable Roles Of Melanin Concentrating Hormone And Orexin On Learned Feeding Behavior Through Optogenetic And Chemogenetic Procedures**

LAUREN RAYCRAFT, NICOLLETTE RUSSELL, RALUCA BUGESCU, GINA LEINNINGER, ALEX JOHNSON
Michigan State University, East Lansing, MI, United States

Within the lateral hypothalamus (LH), both Melanin Concentrating Hormone (MCH) and orexin (ORX) have been described as orexigenic neuropeptides. At the same time, the actions of MCH appear in many ways to contrast to those of ORX (e.g., sleep-awake cycle; glucose sensing). Moreover, GABAergic ORX cells can inhibit MCH cell activity. To examine potential opposing roles played by these two neuropeptides, we used two separate mouse lines where Cre-recombinase was under the control of the Pmch gene (Tg-MCH-Cre) or ORX promoter (ORX-IRES-Cre). Mice received bilateral injections of a Cre-dependent ChR2 into the LH along with implantation of ferrule tips. Following recovery from surgery, mice were trained for cue-potentiated feeding (CPF) in which under conditions of mild food deprivation, mice learned to associate one auditory conditioned stimulus with delivery of sucrose (CS+), whereas a second cue was unpaired (CS-). Mice were tested under *ad-libitum* feeding conditions, where the degree to which each stimulus would evoke CPF was examined. Tests were conducted separately for CS+ and CS-, with four trials of each stimulus presented. Within these tests, laser stimulation (473 nm, 5 ms pulses, 20 Hz) was timed to coincide with stimulus presentation on half of the trials, whereas for the remaining trials no optogenetic stimulation occurred. During stimulated trials Tg-MCH-Cre mice displayed enhanced CPF, whereas stimulation attenuated feeding in ORX-IRES-Cre mice. We also examined the necessity of these two feeding signals in CPF using chemogenetic inhibition via a Cre-dependent hM4Di DREADD. Collectively, our results suggest that within the LH ORX cells may exert direct control over MCH cells, promoting the rapid transition between motivated food-related behaviors.

4:15 **Diet Induced Obesity Alters Orbitofrontal Cortex Astrocyte Function Leading To Impairments In Synaptic Plasticity**

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University of Calgary, Calgary, AB, Canada

The orbitofrontal cortex (OFC) receives sensory information about food and integrates these signals with expected outcomes. Thus, the OFC registers the current value of foods and updates actions based on this information. OFC lesions in animals show a lack of food devaluation. Interestingly, obese humans and rats fed a cafeteria diet have impaired devaluation of food rewards, implicating a potential obesity-induced dysfunction the OFC. Rats were given restricted (1h /day), extended (24h/day) or no (chow only) access to a cafeteria diet. Whole cell patch clamp electrophysiology was used to assess alterations in astrocyte function and synaptic transmission onto pyramidal neurons. Rats became obese after 40- 45 days of extended, but not restricted access to a cafeteria diet. OFC from rats with extended access to a cafeteria diet showed signs of astrogliosis and decreased astrocytic GLT1 transporter currents. This influenced extrasynaptic glutamate leading to enhanced endocannabinoid tone at inhibitory synapses onto pyramidal neurons. Impairments in astrocyte and synaptic function were reversed with N-acetylcysteine. Taken together, these data suggest that astrocyte function and synaptic transmission in the lateral OFC are associated with extended but not restricted access to a cafeteria diet. Thus, obesity can alter function of OFC pyramidal neurons, which may underlie changes to goal-directed food seeking in obesity.

4:30 **Methods To Change Goal-Directed And Cue-Dependent Food Choices**

SABINE FRANK-PODLECH[1,2,3], POPPY WATSON[4,5,6], AUKJE VERHOEVEN[4,5], HUBERT PREISSL[2,3,7,8], SANNE DE WIT[4,5]
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From an evolutionary perspective, eating serves the aim to be satiated and, ultimately, to survive. In our obesogenic environment, however, food-related cues constantly remind us of tasty, unhealthy foods and can trigger unhealthy and habitual food choices. With this study, we aimed to investigate possible ways to change goal-directed and cue-dependent food choices. Previous studies using the Pavlovian-to-instrumental transfer (PIT) task have shown that food-related cues can bias responding towards those same foods. We examined whether goal-directed and cue-dependent choices for an unhealthy (crisps) over a healthy snack (zucchini) could

be reduced (a) following an explicit health vs. palatability mindset induction and/or (b) by logos (cues) that were previously implicitly associated with healthy/unhealthy or palatable/not palatable. The task was conducted in two separate populations of N=102 (76 females) Dutch and N=120 (60 females) German participants. In each population half the sample received an implicit and explicit health mindset induction, the other half an implicit and explicit palatability mindset induction. We could show that cues previously implicitly associated with health mindset changed both goal-directed and cue-dependent food choices towards healthier (health cue) or unhealthier (unhealthy cue) choices. No effect was observed for the palatability condition. In the second population, the effect of gender was investigated systematically, yet, no differential effect for male and females were observed. Thus, both goal-directed and cue-dependent food choices can be changed especially by cues implicitly associated with a health mindset.

4:45 **The Interaction Of Food Insecurity And Food Sensitization**

AMANDA K CRANDALL, AMANDA M ZIEGLER, TEGAN H MANSOURI, ADAM M GRACZYK, JENNIFER L TEMPLE
University at Buffalo, Buffalo, NY, United States

The relationship between food insecurity and obesity poses a significant risk to children, adolescents, and adults as the rates of both obesity and wealth inequality in the US continue to climb. We examined the effects of food insecurity and changes in reinforcing value of food (RRV) after repeated intake of high and low energy density foods (HED & LED) on adolescent body mass index z-scores (zBMI). We hypothesized that the combination of food insecurity and increased RRV of HED food would increase zBMI while increased RRV of LED food would attenuate this effect. All participants, aged 12-14 years (N=224) came to the laboratory for measurements of BMI, baseline RRV, and food insecurity. Participants were provided 14 portions of snack foods to consume once daily, and RRV of HED and LED foods was measured again after two weeks of consumption. Those whose RRV of food remained steady or increased where categorized as sensitizers (SENS). A between-subjects' ANOVA model was calculated with food insecurity status, HED SENS, and LED SENS as independent factors. There was a significant interaction of HED and LED SENS on zBMI, with participants with both HED and LED SENS having higher zBMIs (M=1.12, SE=0.55) than those with HED SENS only (M=-0.12, SE=0.49). When food insecurity was included in the model, the effect of SENS on zBMI was strengthened in that food insecure participants who had HED and LED SENS had significantly higher zBMIs (M=1.60, SE=0.95) compared with HED-only sensitizers (M=-0.81, SE=0.95). These findings suggest that being highly responsive to repeated intake of food in general, as opposed to only HED food, may pose a greater risk of excessive weight in adolescence and that this relationship may be particularly strong in individuals with food insecurity.

5:00 **Repeated Optogenetic Excitation Of Neurons In The Pvn That Express Angiotensin Type 1A Receptors Elicits Cardio-Metabolic Responses: Implications For Stress-Induced Hypertension And Impaired Glucose Metabolism**

KAREN A SCOTT[1], DOMINIQUE N JOHNSON[1,2], EMMA F LODL[1], DEBRA S ARMENDARIZ[2], ANNETTE D DE KLOET[2], ERIC G KRAUSE[1]
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Previous work from our group revealed that angiotensin type-1a receptors (AT1aRs) are expressed on neurons in the paraventricular nucleus of the hypothalamus (PVN) that orchestrate autonomic and neuroendocrine responses to stress. Here, we evaluate whether repeated activation of these neurons recapitulates the cardio-metabolic changes that follow chronic unpredictable stress. Towards this end, we engineered male mice with channelrhodopsin 2 (ChR2) directed to the gene encoding the AT1aR. These mice were implanted with fiber optics targeting the PVN as well as radio-telemetry devices enabling the monitoring of glucose, temperature and cardiovascular parameters. After recovery, mice were housed in the TSE Phenomaster and the effects of optogenetic stimulation on energy expenditure, activity, food and water intake, glucose, and cardiovascular parameters were assessed. Optogenetic sessions lasted 30 min and were conducted twice daily for 10 d. Excitation of AT1aR-expressing neurons in the PVN resulted in immediate increases in blood pressure that quickly returned to baseline at the cessation of optical stimulation. In contrast, stimulation-induced increases in respiratory exchange ratio, oxygen consumption, temperature and glucose were sustained for at least 1h. Intriguingly, stimulation of AT1aR-expressing neurons in the PVN did not significantly affect body weight or overall food and water intake, although acute elevations in food and water intake were observed. These results suggest that the excitability of AT1aR neurons in the PVN may be coupled to cardio-metabolic changes that are observed after chronic stress, and that repeated activation of these neurons may contribute to pathological alterations in cardiovascular function and glucose metabolism.

5:15 **Glucagon-Like Peptide 1 Receptor (Glp1R) Signaling In The Anterior Lateral Bed Nucleus Of The Stria Terminalis (Albst) Recruits A Gabaergic Projection To The Paraventricular Hypothalamic Nucleus (Pvn)**

HUIYUAN ZHENG[1], NADYA POVYSHEVA[2], LINDA RINAMAN[1]
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Stress and metabolism are closely linked. Metabolic and behavioral stress responses are generated, in part, by neural circuits that include the alBST and the PVN, the apex of the hypothalamo-pituitary-adrenal (HPA) axis. We recently reported that chronic suppression of GLP1R mRNA translation in the alBST is anxiolytic in rats, and also reduces the ability of stress to suppress food intake while prolonging stress-induced elevation of plasma corticosterone. Here we hypothesized that GLP1R signaling modulates HPA responses to stress by altering the activity of PVN-projecting alBST neurons. One week after red fluorescent retrobeads were stereotaxically

injected into the PVN in young adult male rats, retrogradely labeled alBST neurons were targeted for whole-cell patch recording in *ex vivo* slices. When the GLP1R agonist Ex4 was bath applied to activate GLP1R's, a depolarizing shift in membrane potential was recorded in PVN-projecting alBST neurons ($p < 0.01$; n=11). Ex4 also increased the frequency of sEPSCs and reduced the frequency and amplitude of mIPSCs. Ex4 effects were eliminated by the GLP1R antagonist Ex9 and also by synaptic blockers, evidence for indirect effects on PVN-projecting alBST neurons. In other rats, cholera toxin B retrograde labeling combined with fluorescent RNAscope *in situ* hybridization confirmed that PVN-projecting alBST neurons are GABAergic (i.e., GAD1 or VGAT mRNA+), but do not themselves express GLP1R. We conclude that GLP1R signaling within the alBST indirectly recruits a GABAergic projection pathway to the PVN, which may contribute to an "inhibitory brake" that constrains stress-induced activation of the HPA axis.

5:30 **(Nita Award Winner)Amylin Signalling In Pomc Neurons Controls Energy Metabolism And Activity**

BERND CU COESTER, THOMAS A LUTZ, CHRISTELLE LE FOLL
Institute of Veterinary Physiology, Vetsuisse Faculty University of Zurich (UZH), Zürich, Switzerland

Amylin, a pancreatic hormone, induces phosphorylated ERK (pERK) in hypothalamic POMC neurons and has a synergetic effect on leptin-induced STAT3 phosphorylation in the arcuate (ARC) and ventromedial (VMN) hypothalamic nucleus. During development, hypothalamic amylin signalling affects axonal outgrowth of agouti-related protein (AgRP) and a-melanocyte-stimulating (aMSH) immunoreactive fibers from the ARC to the paraventricular nucleus (PVN). We hypothesized that amylin directly signals onto POMC neurons to control energy homeostasis and metabolism. In this study, we selectively depleted the calcitonin receptor (CTR) subunit of the amylin receptor in POMC neurons to assess the resulting phenotype in adult mice by crossing tamoxifen (Tx)-inducible POMC-Cre:ER^{T2} mice with CTR-floxed mice. At 4 weeks of age, mice were either treated with Tx or corn oil for 5 consecutive days. Male Tx-treated mice with CTR-depleted POMC neurons (POMC-Cre^{CTR}+Tx) showed an increased body weight gain, increased adiposity and signs of glucose intolerance. Furthermore, POMC-Cre^{CTR}+Tx mice of both sexes had a decreased locomotor activity and energy expenditure when measured over the course of three days. After intraperitoneal injection of salmon calcitonin, an amylin agonist, POMC-Cre^{CTR}+Tx mice did not increase their body temperature during the following 24 hours. The acute effect of amylin on food intake, which is conveyed from neurons in the area postrema over the hindbrain axis, was unaltered in all mice. Density of aMSH fibers in the PVN was the same in all groups. Together, these results show a significant impact of amylin signalling in POMC neurons on energy metabolism and locomotor activity, with a sexual dimorphism.

5:45 **Metabolic Detection Of Energy Deficit By Crat In Agrp Neurons Links Hunger With Reward.**

ALEX REICHENBACH, TARA SEPEHRIZADEH, MICHAEL DE VEER, ZANE B ANDREWS
Monash University, Melbourne, Australia

Obese individuals show increased activation of brain reward regions, and fasting increases the desire to eat in obese more than lean humans. Agouti-related peptide (AgRP) neurons in the arcuate nucleus are one key neuronal population that link homeostatic detection of hunger with dopamine pathways in the brain that control motivation and reward. To assess the role of metabolic sensing in AgRP neurons and the effects on reward and motivation, we studied mice lacking carnitine acetyltransferase (Crat) in AgRP neurons, as our previous studies show that Crat in AgRP neurons plays a crucial role during the metabolic shift from fasting to refeeding. We hypothesized that Crat in AgRP neurons couples the detection of metabolic state with food reward value and motivated behaviors. Two-bottle choice tests show that Crat in AgRP neurons is important for sensing of the caloric value of sweet solutions since fasting increases sucrose consumption in WT more than in KO mice. Moreover, during fasting WT mice will still consume sucrose spiked with quinine (unpleasant tastant) to consume calories as required, whereas KO mice do not. The dorsal striatum mediates the effects of calorie, and not taste, reward processing. Therefore, we developed a whole animal PET/CT f18DOPA scan method to estimate dopamine activity of the dorsal and ventral striatum system. Our results showed lower f18DOPA uptake in the dorsal striatum of KO mice in response to reward stimulus compared to WT mice and no differences in ventral striatum f18DOPA uptake. These studies highlight that Crat in AgRP neurons is crucial for the caloric assessment of sugar solutions and may link the detection of energy deficit with increased dopamine signaling in the dorsal striatum to ultimately impact food reward and motivation.

6:00 - 8:00 PM	Transit Zone
POSTER SESSION III	

P1 **How Full Are You? Mri-Assessed Gastric Content Versus Estimates Of Perceived Fullness Under Free-Eating Conditions**

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Many studies have investigated gastric emptying in relation to subjective perceptions of fullness and appetite. All these studies implicitly assume that people are in some way aware of their gastric content. The objective of this study was to assess how well subjective estimates relate to gastric content under free-eating conditions, and whether this is mediated by interoceptive awareness. Participants (n=84, age 26.9±9.7 y, BMI 22.7±3.0 kg/m^2, F/M=67/17) received no dietary instructions beforehand. Participants completed an interoceptive awareness questionnaire (MAIA - body listening), appetite rating scales (hunger, fullness, prospective consumption, desire to eat and thirst), time since last meal and past 24h food intake. Participants estimated gastric content on a 100-mm VAS (anchors: 'completely empty' and 'so full that it hurts'). Actual gastric content was assessed from stomach MRI images. VAS estimate of content and MRI content were correlated overall, as well as on subsets split by median MAIA score. Overall, estimates of gastric content (36.3±19.5mm) and actual content (219.2±168.8mL) were positively associated ($r=0.58$, $p< 0.001$). MAIA body listening score was 2.3±1.1 out of 5, with a 2.2 median. The association between VAS estimates of gastric content and actual was $r=0.56$, $p< 0.001$ for low and $r=0.60$, $p< 0.001$ for high MAIA participant scores. We confirmed that estimates of gastric content and actual gastric content volume are associated. After this preliminary analysis we will more deeply at the relation between estimation and interoceptive awareness. Further analysis will lead to a full regression model including the macronutrient composition of the meal last consumed and time since the last meal with actual gastric content as a dependent variable.

P2 **Microbiota Theory Of Appetite Regulation**

SERGUEï O. FETISSOV[1,2]

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The homeostatic theory of appetite regulation postulates that the cycles of hunger and satiety are driven by changes of energy metabolism perceived by the brain via signals from energy storage. Although commonly used in academic teaching, this theory cannot explain the mechanisms underlying short-term appetite rhythms consisting of about 20 min of satiation and 5 hours of satiety. Nevertheless, from the bioenergetics point of view, there is little doubt that the energy metabolism should drive appetite cycles. Here, I am presenting the theoretical and experimental evidence that nutrient ingestion-driven energy metabolism of gut bacteria can underlie the host appetite cycles. The energy requirement (1 kcal/g) for the turnover of about 200 g of total bacteria present in human gut as well as their growth dynamics including 20 min of the exponential growth duration are the host independent biological factors which may orchestrate the feeding rhythms. The stationary phase of bacterial growth reflects energy equilibrium state which can be transmitted from gut bacteria to the host and perceived as the feeling of satiety during 5 h of the stationary phase duration. Thus, the synchronized metabolic activity of gut bacteria can be postulated as the primary reason for alternation of host appetite cycles and food intake to satisfy the energy requirements for the continuous renewal of the bacterial population. The microbiota-derived signals are integrated by the brain together with the long-term signals from host energy storage resulting in healthy or altered metabolic and behavioral phenotypes. Finally, recent examples demonstrate that molecular pathways used in microbiota-host communications can be exploited for a design of probiotics aimed at appetite and body weight management.

P3 **Sex Differences In Response To A High Fat, High Sugar Diet: From Gut To Brain**

CAROLINE DALY[1], JUHI SAXENA[1], JAGROOP SINGH[1], RENATA BUFFALINO[1], MARIA MELVILLE[2], LINNEA FREEMAN[1]

[1]Furman University, Greenville, SC, United States, [2]Benedict College, Columbia, SC, United States

Consumption of a high fat, high sugar diet can lead to obesity as well as increased risk of dementia, heart disease, type II diabetes, and stroke. Given the increased consumption of dietary fat, ever-increasing rates of obesity, and the numerous health issues associated with high fat diets and/or obesity in our country, it is imperative to further understand high fat diet-related consequences and their mechanisms. However, there is a gap in our understanding of sex differences in the response to consumption of a high fat diet. Interestingly, female mice are more resistant to diet-induced obesity and have revealed a lack of obesity-induced microgliosis in the hypothalamus. Few studies have investigated sex differences in obesity and sex differences in gliosis (astrocytes and microglia). Furthermore, we are interested in determining peripheral factors that influence diet-induced glial alterations. We hypothesize a role of gut dysbiosis and systemic inflammation to activate astrocytes and microglia. We fed male and female C57Bl/6 mice a high fat, high sucrose diet or control (low fat, low sucrose) diet for 14 weeks and then evaluated weight gain, plasma adipokines and cytokines, and the gut microbiome. Finally, we evaluated microglia and astrocytes in the cortex, hippocampus, and hypothalamus. Our studies reveal sex differences in weight gain, plasma adipokines, and gut microbe populations following consumption of a high fat, high sucrose diet. We also determined a significant effect of diet on astrogliosis in the

hippocampus and hypothalamus, but not in the cortex. Taken together, there are important differences in response to a high fat, high sucrose diet between male and female mice.

P4 **Slow Gastric Emptying Rate For Pearl Millet-Based Foods In Mali Is Not Observed In A U.S. Population, Though Shows A Slow Digestion Property**

ANNA M.R. HAYES, FANNY GOZZI, BRUCE R. HAMAKER
Whistler Center for Carbohydrate Research & Department of Food Science, Purdue University, West Lafayette, IN, United States

Pearl millet-based foods are considered anecdotally to be highly satiating among populations in West Africa and thus have potential to affect ingestive behavior. In a previous clinical trial in Mali, we showed that millet couscous and thick porridge delayed gastric emptying (up to > 5 h half-emptying time) in a normal weight population compared to Western carbohydrate-based foods. The cause of this delay was unknown, but was thought to be related to the ileal brake. We hypothesized that couscous and thick porridge made from pearl millet grown in West Africa would also delay gastric emptying rate in a U.S. population. In a clinical trial conducted in the U.S. with a normal weight population (n=14), gastric emptying, glycemic response, and appetitive response were assessed following consumption of different carbohydrate-based foods (millet couscous - commercial and self-made, millet thick porridge, wheat couscous, white rice) matched on available carbohydrate basis. Results showed rapid gastric emptying rate (< 3 h half-emptying time) for all treatments (p=0.51). Despite lack of differences in gastric emptying, slower initial glycemic rate was observed for millet thick porridge and commercial millet couscous, with lower glycemic response 30-50 min postprandially (p< 0.05), and glucose area under the curve trended higher for white rice. Significant differences were not observed in appetitive response, although for self-made millet couscous hunger ratings trended lower at 0 min (p=0.053) and fullness ratings trended higher at 30 min (p=0.09). Thus, millet foods appear slow digesting, and we propose condition the ileal brake response in Africa, when consumed regularly, perhaps by promoting enteroendocrine cell proliferation to affect gastric emptying and ingestive behavior.

P5 **Glial Cross-Talk Promotes Inflammatory Response In Nodose Ganglia Culture After Exposure To By-Products From Gram Positive, High-Fat Diet Associated Gut Microbes.**

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Vagal afferent neurons (VAN) located in the nodose ganglia (NG) relay gut-derived signals to the CNS to regulate intake. High fat diet (HFD) ingestion alters VAN signaling, potentially via an inflammatory pathway. The gut microbiota may play an important role in diet-driven inflammation. HFD increases gram positive (GP) bacteria abundance in the gut. GP bacteria produce lipoteichoic acid which can activate toll-like receptor-2 (TLR2) on glia and/or neurons and promote inflammation. In this study, we aimed to determine if byproducts of HFD-associated GP bacteria can induce an inflammatory response in cultured NG and the mechanisms involved in this response. NG from Wistar rats were collected, cultured, and treated for 4, 6, or 24 hrs with 50% media in which a HFD-associated GP bacteria were cultured (SUP). 72 hours after plating, cultures were fixed, RNA extracted, and expression of different genes determined via PCR. Treatment with SUP induced a rapid inflammatory response characterized by increased expression of interferon-γ , interleukin (IL)-1β, IL-6, tumor necrosis factor-α and decreased expression of transforming growth factors–α and -β. Bacteria-driven inflammation was blunted by pre-treatment with minocycline, supporting a role for NG microglia in transmitting microbiota-originating signals. Additionally, increased expression of the satellite glia (SG)-produced, microglia-activating genes c-c motif chemokine ligand-2 and lipocalin-2 indicates potential glial cross-talk. Similarly, increased SG-activating vascular endothelial growth factor-B expression suggests microglial promotion of reactive SG. Together, these data suggest that bacterial products can induce a glial-mediated inflammatory response in NG, potentially altering VAN signaling.

P6 **Peptide Yy And Cholecystokinin Mediation Of Prebiotic Fiber-Induced Satiety Is Dependent On Gut Microbiota**

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Prebiotic fiber-induced satiety is correlated with changes in gut satiety hormones and gut microbiota but their causal role has not been established. We determined whether prebiotic fiber modulates gut microbiota and hormones to promote satiety. **Methods:** Male rats were randomized to control high-fat (40% kcal) diet (HFD) with or without inulin fiber (2.5-25%w/w) and monitored for changes in energy balance; antibiotics or fecal microbiota transplant (FMT) were used to manipulate gut microbes. **Results:** Inulin dose-dependently decreased caloric intake, increased CCK and PYY mRNA abundance in cecum and colon, and increased plasma PYY concentrations. Systemic administration of antagonists for CCK-1 (Devazepide) and PYY Y-2 (BIIE0246) receptors attenuated the dose-dependent reduction of caloric intake by inulin in Sprague-Dawley (SD) rats (n=12/group). FMT from donor inulin-fed to recipient HFD fed obese SD rats induced hypophagia and increased plasma PYY concentrations in recipients (n=8). Gut microbiota depletion with antibiotics nullified the hypophagic effects of exogenous CCK and PYY in obesity-prone rats indicating that gut microbiota is important for satiety effects of CCK and PYY (n=12). Inulin promoted hypophagia, weight and adipose losses, increased the number of CCK and PYY immunopositive cells in cecum, and restored healthy gut microbiota in obesity-prone and resistant rats. Notably, CCK and PYY receptor blockers attenuated inulin-induced hypophagia in

control obesity-prone and resistant rats, with very marginal attenuation in antibiotic-treated rats (n=12/strain). **Conclusion**: Prebiotic fibers promote satiety partly through gut microbiota-dependent upregulation of CCK and PYY expression, secretion and signaling.

P7 **The Effect Of Methanandamide On Gastric Vagal Afferent Satiety Signals In Lean And High Fat Diet-Induce Obese Mice.**

STEWART CHRISTIE[1], HUI LI[1,2], REBECCA O'RIELLY[1], AMANDA PAGE[1,2]

[1]Vagal Afferent Research Group, Adelaide Medical School, University of Adelaide, Adelaide, Australia,

[2]Nutrition, Diabetes and Metabolism, Lifelong Health, South Australian Health and Medical Research Institute (SAHMRI), Adelaide, Australia

Gastric vagal afferents (GVAs) relay signals to the hindbrain resulting in sensations of fullness and satiety. Endocannabinoids (ECs) regulate food intake via cannabinoid 1 (CB1) receptors, however, they are also endogenous ligands for transient receptor potential 1 (TRPV1) channels. TRPV1 and CB1 are expressed on GVAs and the EC anandamide (AEA) is expressed in the stomach. This study aimed to determine the relationship between TRPV1, CB1 and ECs in GVA signalling in lean and high fat diet (HFD)-induced obese mice. Male C57BL/6 mice (8wk old) were fed standard laboratory diet (SLD;N=42) or HFD (N=40) for 12wks. An *in vitro* GVA preparation was used to assess methAEA (mAEA; stable AEA analogue) effects on GVA responses to 3g stretch in the absence and presence of a CB1 (rimonabant;300nM)), TRPV1 (AMG9810;30nM), protein kinase (PK)A (Fragment(6-22)amide (F6-22);5nM), PKC (bisindolylmaleimide-II (BIS-II);10nM), Gαi/o (NF023;300nM), or Gαq (YM254890;100nM) antagonist. In SLD mice, low (1-10nM) and high doses (30-100nM) of mAEA reduced and increased GVA responses to 3g stretch respectively; dual effects that were reduced in the presence of both rimonabant and AMG9810. F6-22 and NF023 prevented the inhibitory effect of mAEA. Conversely, BIS-II and YM254890 reduced the excitatory effect of mAEA on GVA responses to 3g tension. In HFD mice mAEA (1-100nM) reduced GVA responses to 3g stretch; an effect blocked in the presence of rimonabant, AMG9810, NF023 or F6-22. In conclusion, ECs acting through CB1 and TRPV1 have a pivotal role in modulation of GVA satiety signals depending on the second messenger pathway utilised. This is lost in HFD-mice where only an inhibitory effect is observed. These changes may contribute to the development and/or maintenance of obesity.

P8 **The Role Of Receptor-Activity Modifying Protein 1 In Amylin&Rsquo;S Control Of Food Intake**

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Amylin is a pancreatic peptide which acts as a key regulator of energy homeostasis. It is co-secreted with insulin by pancreatic β-cells and is involved in many important physiological functions. Amylin is known to predominately bind to three receptors (AMY 1-3) which are composed of the calcitonin core receptor (CTR) and the receptor-activity modifying proteins (RAMP) 1-3, respectively. The objective of this study was to determine the role of RAMP1 in the control of amylin's actions. We hypothesized that in the absence of RAMP1, the anorectic effects of amylin would be absent. WT and global RAMP1-KO mice were fed a chow diet and had comparable basal body weight and food intake (FI). No differences were observed in glucose tolerance between WT and RAMP1-KO mice. All mice received NaCl, amylin (20 ug/kg, 100 ug/kg, 500 ug/kg), and the amylin agonist salmon calcitonin (sCT; 10 ug/kg) in a crossover study. Energy expenditure (EE), FI and respiratory exchange ratio (RER) were monitored. No differences were observed in FI or EE between the WT and RAMP1-KO mice with any of the treatments. When treated with sCT and amylin at 100 ug/kg and 500 ug/kg, the degree to which RER was reduced compared to baseline was blunted in the male RAMP1-KO mice compared to the male WT mice. Mice were perfused 90 minutes following an injection of amylin (50 ug/kg). The area postrema (AP), a region of the brain critical for amylin's control of FI, was sectioned and processed for amylin-induced cFos expression. Both WT and RAMP1-KO mice exhibited robust cFos expression in the AP in response to amylin treatment. Thus, RAMP1 does not appear to be required for amylin-induced satiation or activation of AP neurons; however, differences in RER may suggest that RAMP1 plays a role in energy substrate selection.

P9 **The Role And Regulation Of Amylin Synthesis In The Brain**

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Pancreatic amylin's best-studied physiological function is its strong effect on meal-ending satiation, but it also modulates nutrient utilization and increases energy disposal after weight loss. Two reports show that amylin is also expressed in the brain, in particular in the medial preoptic area, arcuate nucleus (ARC) and lateral hypothalamus. We hypothesize that central amylin is involved in the regulation of energy homeostasis and that its expression is affected by peripheral amylin as well as female sex hormones. Male (15-weeks old 400-420g), female (14-weeks old 300-320g; phase of estrous cycle not known) and lactating female (20-weeks old, 21 days of lactation, 350-370g) Sprague-Dawley rats fed ad libitum were transcardially perfused and fixed. Brain sections were processed for immunocytochemistry to detect amylin expression. Amylin was expressed in the ARC of both male and female rats, but also in the area postrema, which had not been published before. Lactating female rats showed the highest expression of amylin in the ARC amongst the three groups, followed by female and male rats (lactating female rats > male rats ($P< 0.01$), female rats > male rats ($P< 0.05$)). We conclude that central amylin expression has pronounced sexual dimorphism and is affected by stages of reproductive life in females. Ongoing studies will investigate the influence of the estrous cycle on central amylin expression. Furthermore, to reveal the role of endogenous hypothalamic amylin in metabolic control rats will be fasted, fed, exposed to different diets and to peripheral amylin.

P10 **The Effect Of Glucagon-Like Peptide-1 Administration In Brattleboro Rats**

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Long Evans rats that are homozygous for the Brattleboro mutation lack arginine vasopressin (AVP) and are a model of diabetes insipidus. To defend fluid homeostasis in the face of the lack of AVP, Brattleboro rats consume significantly more water than wildtype (WT) controls. Despite this excessive water intake, food intake remains normal. Given that the glucagon-like peptide-1 (GLP-1) system plays a role in satiation of both food and water intakes, it suggests that the impact of endogenous GLP-1 on fluid intake is somehow overridden in the Brattleboro rat, while its role in food intake satiety is maintained. Accordingly, we aimed to use Brattleboro rats to better understand the neural mechanisms regulating water intake, separate from those regulating food intake. As a first step toward this larger goal, we evaluated the response to a central injection of a GLP-1 receptor (GLP-1R) agonist in male and female WT and Brattleboro rats. Food and water intakes were measured 4, 12, and 24 hours post-injection. Preliminary data suggest that despite the strong need to consume water, Brattleboro rats were equally, if not more, sensitive to the GLP-1R agonist exendin-4. This comparison led us to question if GLP-1 suppresses food and water intakes based on raw volume or based on a percent of baseline intake. Additional studies are underway to answer this question and to evaluate proglucagon and GLP-1R expression in brain regions associated with fluid regulation. Although these studies are incomplete, the results to date suggest that Brattleboro rats provide a unique opportunity to examine the endogenous GLP-1 system and its control of fluid intake.

P11 **Mechanisms Underlying Autonomic Effects Of Melanocortin-4 Receptor Agonist**

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Synthetic MC4R agonists have been developed as a therapeutic agent against obesity. It was previously demonstrated that MC4Rs expressed by neurons within the paraventricular nucleus of hypothalamus are responsible for the beneficial effects of MC4R stimulation. However, the expression of MC4Rs by sympathetic neurons resulted in autonomic side effects by the MC4R agonists. To selectively modulate anorexigenic effect, it is essential to understand the mechanisms underlying autonomic regulation by MC4R. In the present study, we investigated cellular mechanisms responsible for MC4R regulation of sympathetic preganglionic neuronal activity. Using ChAT-IRES-Cre::tdTomato mice model, we recorded neuronal activity of sympathetic preganglionic neurons in the intermediolateral column (IML). We found that MC4R agonists either depolarize or hyperpolarize IML cholinergic neurons in a PKA-dependent manner. We also performed a series of experiments to study the molecular identity of non-selective cation channels activated by MC4R stimulation. Together, our results represent cellular mechanisms responsible for the autonomic effects of MC4R agonists, which should help to develop novel and safe anti-obesity drugs.

P12 **No Evidence That Central Leptin Signaling Modulates The Acquistion Or Expression Of Flavor-Nutrient Learning.**

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In flavor-nutrient learning, rats acquire strong preferences for flavors accompanied by postingestive nutrient sensing. This learning steers choice and promotes intake of energy dense foods. Prior research is mixed regarding how short-term energy deprivation and long-term energy balance influence this type of food reward. The current work investigated whether manipulations of central leptin affect rats' ability to learn a novel flavor-nutrient association or to express a previously learned association. Ten rats with lateral ventricle cannulas and intragastric catheters were trained in a flavor-nutrient learning paradigm. Each rat was trained with four distinct non-nutritive flavors in saccharin in a series of 30 min/day sessions. Two flavors (CS+) were accompanied by IG infusion of glucose, and two (CS–) were paired with IG water. Of those, one CS+ and CS– were trained after ICV leptin infusion (4μg) and the other CS+ and CS– after ICV saline. Preference learning was assessed in post-training 2-bottle tests. Rats strongly preferred each CS+ over the respective CS– regardless of leptin treatment during training, indicating that central leptin does not modulate acquisition of flavor-nutrient associations. Further 2-bottle testing found ICV leptin at the time of testing did not attenuate rats' previously acquired CS+ preference. Thus we conclude that both acquisition and expression of flavor-nutrient learning are relatively insensitive to central leptin levels.

P13 **Beneficial Effects Of Leptin Antagonism On Glucose Homeostasis In Diet-Induced Obese Mice**

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Obesity is characterized by high circulating levels of leptin and a state of chronic low-grade inflammation. Recent studies have shown that pro-inflammatory signaling in the hypothalamus provokes a decrease of central

leptin and insulin action associated with impaired glucose tolerance. Intriguingly, leptin not only regulates body weight and glucose homeostasis but also acts as a pro-inflammatory cytokine. Consequently, we hypothesized that hyperleptinemia may contribute to the manifestation of chronic low-grade inflammation leading to impairments in glucose tolerance. To test this hypothesis, we chronically administered different doses of a long-acting (pegylated) leptin antagonist (PESLAN) in mice fed a high-fat diet (HFD) to block excessive leptin action during diet-induced obesity (DIO). The initial use of a high dose of PESLAN further exacerbated the body weight gain induced by HFD and worsened glucose intolerance suggesting a substantial inhibition of leptin signaling and ongoing glucoregulatory action of the hormone during DIO. Using lower doses, chosen to block excessive leptin action while basic action is maintained, revealed an opposite effect and improved glucose tolerance significantly without affecting body weight. Immunohistochemical analysis of mouse brains treated with the low dose revealed a significant reduction in the number of both microglia and astrocytes in the arcuate nucleus of the hypothalamus. Our results suggest that excessive leptin action may increase pro-inflammatory signaling and thereby contributes to glucose intolerance during DIO. Lower doses of PESLAN partially but not fully restored glucose tolerance suggesting that removing hyperleptinemia is only one part of the puzzle to potentially treat DIO-induced glucose intolerance.

P14 **Mechanisms For Anorexia By A Novel Glp-1 Receptor Agonist**

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Glucagon-like peptide-1 (GLP-1) is known for its potency in reducing food intake and body weight as well as normalizing blood glucose levels. However, the neurobiological basis of such anorectic action has not been established. Using a novel GLP-1 analog, exendin-4 (1-32) K–capric acid (Ex-4-cap), we investigated the neuronal substrates for mediating the anorexgenic effects of GLP-1 receptor activation. We found that the central injection of Ex-4-cap in C57BL/6J mice induced anorexia at 6-12 weeks of age, and that the presence of pro-opiomelanocortin (POMC) neurons are essential in mediating the action. The ex vivo electrophysiological measurements revealed that the Ex-4-cap directly stimulates the POMC neurons in the arcuate nucleus of hypothalamus mostly via closure of ATP-sensitive potassium (K-ATP) channel in a PKA-dependent pathway. Collectively, we expect our findings of central mechanisms and the cellular phenotypes for mediating the anorectic actions of Ex-4-cap to provide an insight for future anti-obesity drug development.

P15 **Characterization Of The Parasubthalamic Nucleus As An Appetite Suppression Center**

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The motivation to eat depends on the relative balance of activity in orexigenic and anorexigenic neuronal populations. Here, we describe a relatively unexplored population of neurons in the parasubthalamic nucleus (PSTN) that suppresses appetite. We show that PSTN neurons can be subdivided into populations of neurons that express either tachykinin 1 (Tac1) or corticotropin releasing hormone (CRH). Tac1 PSTN neurons, but not CRH PSTN neurons, increase activity following a meal or after administration of anorexigenic hormones. Stimulation of Tac1 PSTN neurons decreases food intake while stimulation of CRH PSTN neurons has no effect on feeding. Tac1 PSTN neurons project to the external lateral parabrachial nucleus and nucleus of the solitary tract, two brain areas that contain anorexigenic neuronal populations, suggesting a potential mechanism for their suppression of food intake. Taken together, Tac1 PSTN neurons serve as a key anorexigenic neuronal population.

P16 **Metabolic Consequences Of Individual Housing In Male C57Bl/6J Mice After Weaning**

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Rodent studies which model human disease and/or treatments differ widely in study design, with varying (social) housing conditions depending on e.g. type of data collected and local husbandry practices. While individual housing can lead to chronic psychosocial stress it also prohibits social thermoregulation. Together, these factors may modulate metabolic health. In the current study we have characterized the metabolic consequences of individual vs social housing of male C57Bl/6J mice. This was achieved by housing mice either individually (IND) or socially (SOC; n=2 siblings/cage) in a temperature-controlled room (21±2°C) from weaning onwards. Body weight (gain) was monitored and energy intake and expenditure were determined using indirect calorimetry during adolescence and adulthood, under normal and (adult) high fat diet conditions. Femur length, body composition and plasma hormones were determined at 6 and 18 weeks of age. This resulted in increased caloric intake and energy expenditure in individually housed mice. While growth rate was reduced during adolescence, weight gain of IND exceeded that of SOC in adulthood. At both life stages, however, IND showed higher adiposity and reduced bone length compared to SOC, with plasma hormones matching this phenotype. Adult exposure to high fat diet further amplified these differences. This shows that Individual housing of male mice under standard laboratory temperature affects energy balance regulation and metabolic health outcomes. These factors have the potential to influence other experimental outcomes used in mouse models of human disease. Increased awareness and understanding of the metabolic consequences of rodent housing practices can support reproducibility and translation of study results.

P17 **Determining The Effects Of Environmental Sustainability Labels On The Selection, Purchase, Or**

Consumption Of Foods: A Systematic Review Protocol

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Environmental sustainability labels (ecolabels) provide an indication of the sustainability of a product and may guide consumers to make environmentally conscious decisions. To date, the impact of ecolabels on consumers' demand for more environmentally-conscious foods has not been systematically explored. This review aims to explore the effects of ecolabels (logos or claims) on consumers' selection, purchase or consumption of food and drink products. Studies will be identified from searches of seven electronic databases (Cochrane Central Database of Controlled Trials, CAB Abstracts, Embase, PsycINFO, Science Citation Index, MEDLINE, and Dissertations & Theses) based on methods in the Cochrane Handbook for Systematic Reviews and Interventions. Two independent researchers will screen papers to determine inclusion and perform data extraction and quality assessment in duplicate. Any type of experimental intervention study written in English will be included. Papers reporting non-experimental analytical studies or qualitative studies will be excluded. Due to expected heterogeneity between study design and intervention type, a non-meta-analytic approach will be used to summarise the results and to allow for comparisons to be made between sub-groups of ecolabels. This protocol is registered on Prospero (CRD42018087635). By capturing the effects of ecolabels in both intervention and comparison groups, this review will provide more accurate estimates of the effectiveness of ecolabels as drivers of sustainable consumer behaviour, specifically with regard to food and drink products.

P18 **Role Of Macronutrient Intake In Improvement Of Metabolic Syndrome Markers In Subjects With Obesity; A Meta-Analysis Of Low-Carbohydrate And Low-Fat Diet Interventions.**

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The metabolic syndrome (MetS) is a cluster of cardiometabolic risk factors found in individuals with obesity, which frequently escalates in cardiometabolic diseases like diabetes and stroke. Dietary guidelines to prevent or turn-around progression of MetS suggest using a low fat (LF) diet, however, low carbohydrate (LC) diets have recently gained attention too. The mechanisms underlying MetS resolution by LC and LF diets presumably include a combination of weight loss, caloric intake reduction, and/or changes in macronutrient intake, but their relative contributions are not known. To unravel these mechanisms, we performed a meta-analysis of studies about subjects on LC and LF diets, and subsequently performed regression analysis with MetS parameters as dependent variables and abovementioned factors as independent variables. A PubMed search yielded 17 articles describing 12 separate interventions assessing changes in body weight, macronutrient/caloric intake and MetS markers of obese subjects without cardiometabolic disease diagnosis assigned to LC or LF diets over a period of 6 and 12 months. While both LC and LF diets reduced body weight significantly, meta-regression analyses revealed that lowering carbohydrate relative to fat and protein intake, but not changes in caloric intake, significantly explained improvements in several markers of MetS. Because these effects appeared independent of MetS improvements by diet-induced weight loss, it is concluded that differential pathways exist by which changes in macronutrient intake and weight loss can lower MetS parameters.

P19 **A High Fat Diet Suppresses Body Weight Defense Mechanisms Through Post-Ingestive Effects**

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Body weight is defended in mammals so that increases or decreases in weight activate responses that favor a return to the initial weight. However, obesity rates and average body weight have been rising over the past several decades. Multiple factors have been implicated in this rise in body weight, including increased consumption of highly palatable, calorically dense foods. We hypothesize that consumption of palatable, high-fat foods suppresses body weight defense mechanisms allowing weight gain to occur. We have created an intragastric feeding paradigm in mice whereby we can to rapidly induce weight gain of roughly 40% of the initial body weight. (Ravussin et al., Cell Met *28*, 289-299.e285, 2018). This paradigm allows us to study the physiologic system that defends against weight gain and to test whether a palatable diet can suppress this system. Using a series of preference tests, we found that sweetened diets are more palatable to C57BL/6J male mice than unsweetened diets, yet the preference for sweet taste was not sufficient to increase caloric intake or body weight. However, we found that increasing the fat content of a diet increases both palatability and consumption (9.81 ± 1.03kcals vs. 14.61 ± 1.03kcals) leading to weight gain. Moreover, we found that a high fat diet attenuates the defense against overfeeding induced weight gain by suppressing the hypophagic response which normally facilitates a return to initial body weight following overfeeding. This attenuation of weight defense is independent of palatability, as increased caloric intake is also induced by intragastric infusion of a high fat diet, which suggests that the post-ingestive effects of a high fat diet are at least partially responsible for the ability of a high fat diet to induce weight gain.

P20 **Can'T Decide How Much To Eat? Variability Of Behavior In Hedonic Eaters**

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Problematic eating can manifest itself in the alternation of restricted food intake and over-indulgence in the form of binges. Formally, this eating pattern can be conceptualized as more variable than homeostatic eating and previous research has shown that this is associated with more variable brain responses to food reward (Kroemer et al., 2016, NeuroImage). Here, we reasoned that non-homeostatic eating would be associated with higher variability in reward seeking as captured by an effort allocation task (EAT). To test this hypothesis, 41 healthy, overnight-fasting participants (MBMI = 23.0±2.9 kg/m2) had to work to earn food and monetary rewards by exceeding required levels of relative button-press frequency. Participants completed the EAT twice, once during sham and once during transcutaneous stimulation of the vagus nerve. Analogous to previous work, we calculated variability as the standard deviation of EAT model residuals. As expected, greater variability in reward seeking was associated with higher scores on questionnaires reflecting hedonic eating. A cross-validated elastic net prediction model identified the Yale Food Addiction Scale, the Food Present subscale of the PFS, the Susceptibility to Hunger subscale of the TFEQ, and general reward sensitivity (Behavioral Activation Scale) as best predictors of variability. We conclude that more variable reward seeking may reflect greater volatility in reward representations, which might be a risk factor for problematic eating behavior. More broadly, reward volatility could be linked to uncertainty of prospective rewards and we outline how incorporating uncertainty into experiments can unravel basic mechanisms that may ultimately help to better understand what is driving binges.

P21 **Evidence For A Transition From Goal-Directed To Habit Associated Neural Circuitry After Binge-Like Eating In Mice**

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Binge eating (BE) is a core eating disorder behavior, but there is limited understanding of neural circuit abnormalities contributing to the persistence of BE. Corticostriatal circuitry associated with goal-directed (prelimbic cortex [PL], dorsomedial striatum [DMS]) and habitual behavior (infralimbic cortex [IL], dorsolateral striatum [DLS]) has been implicated in BE, and changes within this circuitry during the transition from acute to chronic BE may contribute to BE maintenance. Therefore, we first investigated whether intermittent access to palatable food (PF) led to binge-like eating in mice. We then examined whether persistent BE was associated with changes within corticostriatal circuitry. Adult C57Bl/6J mice (N=47) were assigned to intermittent (daily 2-hour, 3x/week 2-hour) or continuous PF (sweetened condensed milk) access schedules. After a 2-week acute phase, there was an overall effect of schedule ($F(1,19)=14.17$, $p< .001$) such that intermittent access animals consumed more PF than continuous access animals ($p's< .03$). Intermittent BE patterns were re-established after each of 3 reinstatement testing periods, suggesting chronic neural changes. Daily intermittent access animals showed significant correlations in cFos levels between PL/IL and PL/DLS ($p's< .05$) after the acute phase, providing initial evidence for a transition from goal-directed to habit related circuitry over time after intermittent binge-like eating. Ongoing experiments are using dual color *in vivo* fiber photometry to quantify neural activity patterns in the IL/DLS time-locked to specific BE behaviors during acute to chronic BE progression. Findings provide evidence that intermittent PF access schedules, similar to human BE patterns, lead to a shift towards engagement of habit related circuits.

P22 **Satiation Is Associated With Increased Connectivity Between Reward And Cognitive Control Brain Areas: An Fmri Study.**

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This study tested the hypothesis that metabolic signals may have effects on food reward processing via alterations in higher cognitive function, using functional magnetic resonance imaging (fMRI). Twenty-seven

subjects (10/17 male/female; mean BMI = 22 kg/m^2; mean age = 21y) participated in two separate test days in a counterbalanced order. The same battery of tasks was performed on both days, but on one day participants were tested after eating a meal to satiation (satiated condition) and on the other day they were tested after not eating for 4h (pre-meal condition). Participants first completed an fMRI scan while they viewed images of high and low calorie foods, and non-foods. After the scan, a money and food-based delayed discounting task was completed: participants had to hypothetically choose between a certain amount of money/food now versus a larger amount later. Food images (but not non-food images) were rated as less appealing in the satiated compared to the pre-meal condition ($p < 0.001$). Choice of a delayed food reward was increased in the satiated condition ($p < 0.005$), but there was no effect on monetary reward ($p = 0.9$). A psychophysiological interaction analysis revealed that when exposed to high versus low calorie food images, there was stronger connectivity between the dorsolateral prefrontal cortex (dlPFC) and ventromedial prefrontal cortex (vmPFC) in the satiated versus the pre-meal condition (FWE-corrected $p < 0.05$). These results suggest that satiation shifts preference from immediate to future food rewards. Moreover, natural satiation is associated with increased functional connectivity between reward-processing (vmPFC) and cognitive control (dlPFC) areas; a connection associated with behavioural-control in eating behaviour.

P23 **Interaction Of Dopamine Depletion And High-Fat/Sugar Diet On Reinforcement Learning And Working Memory In Humans**

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Dopamine is important for cognitive control and feedback learning, processes altered in humans with obesity, which is among others caused by high fat and sugar diet (HFS). In animals, HFS alters dopaminergic signal transmission in cognition-related brain regions. Using dopamine depletion, we probed the influence of low fat/sugar diet (LFS) and HFS on dopamine-mediated cognitive functions in humans. Healthy, female participants were divided into LFS (n=37) or HFS group (n=28) based on the Dietary Fat and Free Sugar Questionnaire, matched for BMI and IQ. We analyzed levels of amino acids, metabolic hormones and parameters of fat and sugar metabolism. To test the differential effect of manipulating brain dopamine levels between groups, participants performed a reinforcement learning (RL) and a working memory (WM) task both with and without acute dopamine precursor depletion (ADPD) prior testing. Both groups showed similar levels of metabolic hormones, but HFS resulted in increased cholesterol and glycated hemoglobin. Furthermore HFS was associated with a higher Phe+Tyr to large neutral amino acid ratio, reflecting higher central dopamine.WM performance did not differ between groups, but lowering central dopamine levels after ADPD impaired WM performance in the LFS (n=17), but not the HFS group (n=14). Performance on the RL task was not affected by the intervention and did not differ between groups (n_{LFS}=12, n_{HSF}=11). Our results show that the two diet groups are distinct in parameters of fat and sugar metabolism and the amino acid ratio suggests higher central dopamine availability in the HFS group. Decreasing dopamine levels reduced WM performance specifically in the LFS group, suggesting differential dopaminergic transmission due to long-term fat and sugar consumption.

P24 **Unaware Of The Amount Consumed: Systematic Error In Food- And Drink Intake Estimation**

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High caloric food products that can be easily consumed lead to overconsumption due to insufficient perception (oro-sensory exposure, OSE) of the amount consumed. Better perception and thus awareness of the amount consumed may help control food intake. The aim of this study was to determine whether OSE duration, taste category and portion size influence the error in estimated intake (EiE). Subjects (n = 72) were recruited at a science festival were they participated in an experiment. The study had a 2x2x3 design with a reference condition (water). Experimental conditions differed in OSE duration through texture (liquid vs. solid stimuli), in taste category (savory vs. sweet) and in portion size (small, medium, large). Participants consumed a drink and a food product of the same portion size category in a blinded manner. Then they were asked to estimate the amount by pouring the same products in an empty cup. Participants overestimated the amount consumed of all stimuli. Overestimation was ten times greater for solid compared to liquid products (104±12 vs. 12±9 %) and was larger for sweet (75±9%) than savory products (41±12%). In addition, there was a trend for larger EiE% of smaller portions. People overestimate the amount they consume of solid and sweet products more than that of liquid and savory products. This may be due to overvaluation of the oro-sensory stimulation when visual cues and intake effort are limited. Future research may study whether overestimating leads to lower intake at a following meal.

P25 **Parents Report Greater Concern For Increased Weight In Girls Than In Boys**

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As childhood obesity rates continue to increase, it is critical to understand how child-level characteristics may differentially affect risk for this disease. Obesogenic eating behaviors and parental feeding practices have been shown to differ by child sex and weight status, however, little is known about how these factors interact. To better understand the relationship between age, child weight status, sex, and parental feeding attitudes, we examined parent report on the Child Feeding Questionnaire from 11 completed data sets. A total of 255 (M=129; 50.6%, 70 with overweight/obesity) children ages 3-12 years were used in the analysis. Because of the greater societal emphasis on “thinness” for females than males, we hypothesized that parents would report greater concern with increased weight status for girls than boys. Hierarchical Regression Models were used to test the interactive effects of child sex, age, and parental concern on children’s weight status. A quadratic effect of age was found showing that parent concern for child weight began to increase with age after the child was 7.5 years-old. Additionally, a significant sex*weight group (P=0.015) interaction was found such that parents reported greater concern for children with overweight and obesity compared to children with healthy weight, and the difference between weight groups was greater for girls than boys. Age did not interact with sex or weight group. These data suggest that the development of overweight or obesity elicits greater concern from parents of girls than boys. These findings provide further support of sex differences in the parent-child feeding relationship that may have implications for the development of personalized interventions to prevent excess weight gain.

P26 **A Systematic Review And Meta-Analysis Of The Social Facilitation Of Eating**

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People tend to eat more when eating with other people compared with when they eat alone, and this is known as the social facilitation of eating. However, little is known about when and why this phenomenon occurs. This review quantifies the evidence for social facilitation of eating and identifies moderating factors and underlying mechanisms. We systematically reviewed studies that examined food intake/food choice as a function of the number of co-eaters. Studies that used naturalistic techniques were narratively synthesized. Meta-analyses were conducted to synthesize results from experimental studies. We reviewed 41 studies and found strong evidence that people eat more when eating with friends compared with when they eat alone,Z= 5.80, p < .001. The meta-analysis revealed no evidence for social facilitation across studies that examined food intake when participants ate with strangers, Z=1.21, p< .230. There was some evidence that social facilitation of eating is moderated by gender, weight status, and food type. However, lack of research prevented an assessment of these variables in participants who only ate with friends. Findings suggest that the social facilitation of eating may be partly mediated by longer meal duration and perceived ‘appropriateness’ of eating. To conclude, findings suggest that eating with others increases food intake relative to eating alone, and this is moderated by the familiarity of co-eaters. The review identifies potential mechanisms for social facilitation of eating and highlights the need for further research to identify mediating factors. Finally, we propose a theoretical framework in which the social facilitation of eating can be regarded as an efficient and necessary evolutionary adaptation.

P27 **Psychological Predictors Of Overconsumption In Response To A Day Of High Energy Density (Hed) Meals In Women Engaged In A Weight Loss Attempt.**

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It is generally accepted that loss of control of eating may undermine long-term weight loss. Given the high availability of HED foods in the obesogenic environment, it is important to identify individuals most susceptible to overconsumption of HED foods during weight loss attempts. This study examined psychological predictors of overconsumption in response to HED meals during a weight loss attempt. Women (n=96) who had voluntarily enrolled in healthy eating-based weight loss programs were recruited [analysed n=81; 41.9±1.4 years; 34.1±0.4 kg/m^2]. Body weight was measured in weeks 1 and 14. After a two-week run-in period, resting metabolic rate (RMR) and psychometric eating behaviour traits were assessed (restraint, disinhibition, hunger, flexible, rigid, binge eating and craving control). Participants attended a day in the laboratory and were provided with fixed and *ad libitum* HED meals (>2.5 kcal/g). A fixed breakfast and lunch provided 50% of estimated individual daily energy requirements [estimated at 1.4xRMR] and participants consumed an *ad libitum* evening meal and snacks. The percentage (%) difference between total daily energy intake and estimated daily energy requirements determined overconsumption. On average participants overconsumed by 33±5% (550±88 kcal). Linear regressions showed that low craving control was the only psychometric trait that significantly predicted overconsumption (R^2=.20, p=.04). Overconsumption on the HED day (β=.23, p=.005) was a significant predictor of %weight change at week 14, alongside %weight change during the run-in period (β=0.65, p< .001; R^2=.49, p< .001). These findings highlight the importance of identifying those susceptible to food cravings and developing strategies to manage cravings for HED foods during weight loss attempts.

P28 **The Role Of &Lsquo;Feeling Fat' In Emotional Eating: A Serial Mediation Model**

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Feeling fat is a transient yet common experience characterised by physical sensations of fatness irrespective of actual weight. Feeling fat may be linked to the inability to correctly identify and label emotions and bodily sensations, which are documented features of alexithymia and poor interoceptive awareness. Pink et al. (2019) put forward a model exploring the role of alexithymia and interoceptive awareness in emotional eating. Here, we propose an extended model of emotional eating incorporating deficits in emotional processing, poor interoceptive awareness as well as the sensation of feeling fat. Healthy female participants (N=241; age: M=24.18 years, SD=7.58; BMI (available for n=164): M=24.04, SD=4.18) completed an online questionnaire containing the Toronto Alexithymia Scale (TAS), the Feeling Fat subscale (FF) of the Body Attitudes Questionnaire, the Multidimensional Assessment of Interoceptive Awareness (MAIA) and the Emotional Eating subscale of the Dutch Eating Behaviour Questionnaire. Feeling fat was significantly and positively correlated with alexithymia (r=.226, p< .001), emotional eating (r =.361, p< .001) and BMI (r=.266, p< .001). Several significant correlations between alexithymia and feeling fat were also found with subscales of the MAIA; the strongest being with trusting ones bodily sensations (TAS: r=.337, p< .00; FF: r=-.406, p< .001). A serial multivariate mediation model revealed alexithymia had a significant indirect effect on emotional eating, via trusting and feeling fat, B=.0034, CI=.0011-.0072. These findings suggest that poor emotional processing combined with a lack of trust in bodily sensations may lead to the sensation of feeling fat, which in turn drives emotional eating.

P29 **Power Of Mind: Attentional Focus Rather Than Palatability Dominates Neural Responding To Visual Food Stimuli**

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The precise role of the mesocorticolimbic system in neural processing of food stimuli remains unclear. Crucially, high-caloric palatable foods have a double-sided nature; they are often craved but also associated with being unhealthy. Therefore, neural responses to individually tailored palatable and unpalatable high caloric food stimuli were measured, while female overweight participants' (n = 23) attentional focus was manipulated to be either hedonic or neutral. Interestingly, the mesocorticolimbic system did not respond significantly differently to palatable than to unpalatable food stimuli. Instead, independent of food palatability, several regions in the mesocorticolimbic system responded more strongly when attentional focus was hedonic than when neutral. Multivariate analyses showed that food palatability could be specifically decoded when participants' attentional focus was hedonic. Our findings show that activity in the mesocorticolimbic system is not proportionate to the palatability of foods, and underline the importance of considering attentional focus when measuring food-related neural responses.

P30 **The Dot Probe Task As A Measure Of Attentional Bias Towards Food Stimuli: An Event-Related Potential Analysis**

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Attentional biases towards food have been theorized to contribute to both weight status and dietary decisions. This theory has not been examined using the dot probe task in conjunction with event-related potentials (ERP). Thus, this study aimed to evaluate measures of behavioral and ERP biases, and reliability of each of these outcomes. Additionally, these measures were examined in relation to self-report measures of attitudes towards food. 53 adults ages 18-44 (17 M) completed the Power of Food Scale, the Eating Attitudes Test-26, as well as a novel dot-probe paradigm comparing food vs. neutral stimuli for measures of behavioral (accuracy, reaction time interference [RTI]) and neuroelectric (mean amplitude of the N2pc) outcomes. Body Mass Index (BMI) was used to assess weight status. HEI-2015 was used to assess diet quality. Correlations were conducted between behavioral, N2pc, surveys, diet, and BMI. Split-half reliability comparisons were conducted amongst the first and second trial blocks to assess for task reliability. No significant difference was observed between the N2pc contra nor ipsi-lateral to food stimuli (p=0.86). No relationship was observed between the N2pc and BMI (p=0.85). Similarly, no relationship was observed between BMI (p's>0.26), diet (p's>0.14) nor the surveys (p's>0.08) and the N2pc nor RTI. There was no difference between RTI nor N2pc mean amplitude across trial blocks (p's>0.21), indicating good task reliability. No attentional biases towards food stimuli over neutral stimuli were observed among a healthy sample of participants with varying BMI's. Reliability measures indicated good reliability for all outcomes. Thus, this task may be used in future studies amongst populations more vulnerable to attentional biases towards food stimuli.

P31 **Galangin Stimulates Glucagon-Like Peptide-1 Secretion In Enteroendocrine Cells Via Sweet Taste Receptor-Dependet And -Independent Pathways**

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Glucagon-like peptide-1 (GLP-1), a hormone secreted from enteroendocrine cells, is involved in the regulation of energy homeostasis. An approach is useful to increase endogenous GLP-1 secretion through modulation of the secretory mechanism in enteroendocrine cells by pharmaceutical agents or dietary ingredients. Galangin is a 3,5,7-trihydroxyflavone with molecular formula $C_{15}H_{10}O_5$, is a principal constituent of honey and propolis. There have been studies on the regulatory functions of galangin on energy homeostasis. In the present study, it was demonstrated that galangin significantly increased GLP-1 secretion in enteroendocrine NCI-H716 cells. Concerning the secretory mechanisms, the increase in GLP-1 secretion by galangin involved the sweet taste receptors (STR)-dependent pathway, from the experiments using transfection of siRNA for TAS1R2 and TAS1R3 in NCI-H716 cells. Also STR-independent pathways was involved from the experiments using a pharmacological blocker (phloridzin) for sodium-dependent glucose co-transporter 1 (SGLT1) and a blocker (cytochalasin B) for glucose transporter 2 (GLUT2). As sugar detectors (SGLT1 and GLUT2) in the gut might to be involved in the reachment of gut appetition signals to the brain, the STR-independent pathways of galangin-induced GLP-1 secretion might hold the possibility of the regulation of postoral ingestive behavior.
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P32 **Age, Gender, Ethnicity And Eating Capability Influence Oral Processing Behaviour Of Liquid, Semi-Solid And Solid Foods Differently**

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Food oral processing depends on food properties and consumer characteristics. The aim of this study was to determine the effect of age, gender, ethnicity and eating capability on oral processing behaviour of liquid, semi-solid and solid foods. Oral processing behaviour of 18 commercially available foods, ranging from liquids, semi-solids to solids, was compared between Dutch, Caucasian adults (18-30yrs), Chinese, Asian adults (18-30yrs), Dutch, Caucasian elderly (60-80yrs), and consumers with mild, swallowing problems and/or low mastication efficiency (18-80yrs). Participants were video recorded during food consumption and six oral processing parameters extracted. Elderly consumed all foods with lower eating rates than young adults by increasing consumption time. Females consumed solid foods with lower eating rates than males by reducing bite size. Chinese, Asian consumers consumed liquid and solid foods with lower eating rates than Dutch, Caucasian consumers by reducing bites size. Chinese, Asian consumers consumed semi-solid foods with lower eating rates than Dutch, Caucasian consumers by reducing bite size and increasing consumption time. Consumers with decreased mastication efficiency or mild swallowing problems showed similar oral processing behaviour than healthy consumers, probably because reduction in eating capability was limited in the group. This demonstrates that different consumer groups adapt eating rate in different ways by modifying bite size, consumption time or both. To conclude, age, gender and ethnicity influence oral processing behaviour of liquid, semi-solid and solid foods differently. This study assists in steering sensory perception, food choice and energy intake of specific consumer groups such as the elderly.

P33 **Novel Glucose Sensing Mechanism(S) In The Murine Taste System**

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Mice given the opportunity to experience the sensory and metabolic effecs of glucose and fructose—two sugars that bind to the same Trpm5-affiliated taste receptor (T1R), but are metabolically distinct—come to respond more positively to the orosensory properties of glucose, suggesting there may be an alternative glucose taste receptor. Proteins associated with glucose sensing in other tissues [e.g., sodium-glucose linked transporter (SGLT1/3), metabolic sensor components] are found in taste cells, but their functions have not been fully elucidated. We sought to determine if such sensors contributed to taste-based motivation for glucose in sugar-naïve (n = 8) and sugar-experienced (n = 7-8) B6 mice using a series of 20-minute brief access taste tests (10-s trials, randomized order) with various sugar solutions and non-metabolizable glucose analogs. Sugar-experienced B6 mice licked selectively more for sugars containing glucose, 2 deoxyglucose (2DG) and L-glucose, but not alpha-methyl glucopyranoside, a SGLT1/3 ligand. The patterns of licking further indicated the alternative glucose signal may interact with the canonical "sweet" taste signal. Thus, a similar series of brief access tests were conducted on sugar-experienced mice lacking the functional T1R pathway (Trpm5 knockout, KO, n = 6) and their wildtype (Trpm5 WT, n = 9-10) counterparts. Like B6, KO and WT mice displayed increased licking responses to the orosensory properties of glucose and glucose-containing sugars. Together, these findings suggest that experience-dependent avidity for glucose taste does not require input from the GPCR-linked taste pathway and does not involve SGLT1/3; however, 2DG and L-glucose mimicking glucose points to a novel metabolism-independent glucosensor in the murine taste system.

P34 **Recovery From Sucrose-Induced Cognitive And Metabolic Impairments In Both Male And Female Rats.**

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The aim of this experiment was to compare male and female rats in terms of metabolic and cognitive impairments produced by excessive intakes of 10% sucrose solution and in terms of recovery once access to sucrose ceased. The primary cognitive outcome was performance on a place recognition task. The primary metabolic outcome was retroperitoneal fat pad mass at cull, with body weight and glucose tolerance as secondary outcomes. In a 3 x 2 between-subject factorial design over two stages the first factor was whether rats had unlimited access to a 10% sucrose solution and water throughout both stages (*S-S*), were switched from sucrose in the 8-week Stage 1 to water only in the 4-week Stage 2 (*S-W*) or had no access to sucrose in either stage (*W-W*). The second factor was sex. Animals had unrestricted access to chow throughout. There were 10 female and 10 male rats in each of the three conditions. At the end of Stage 1 place recognition was impaired in *S-S* and *S-W* rats ($F(1, 51)= 70.2$, $p< 0.001$). At the end of Stage 2 place recognition was still impaired in *S-S* rats ($F(1, 53)= 44.9$, $p< 0.001$), while it had fully recovered in *S-W* rats. No interactions with sex were found ($ps>0.10$). On the other hand, the primary metabolic outcome, fat pad mass, revealed that, while switching from sucrose to water led to complete recovery in females (no difference between *S-W* and *W-W* conditions; $p>.10$), in males fat pads in the *S-W* group did not differ from those in the *S-S* group ($p>.10$). In conclusion, despite females drinking more sucrose relative to body weight than males, the only sex difference detected in terms of impact of excessive sucrose and recovery when sucrose was withdrawn was persistence of adiposity in males but not in females.

P35 **Effects Of L-Arabinose On Glycaemic Response, Satiety And Body Weight In Humans: A Literature Review**

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High sugar consumption increases blood glucose levels which may lead to increased risk for type II diabetes. Approaches that improve postprandial glycemic response, such as sugar reduction, would help address this, and may also lead to more satiety and better weight management. Besides sweetening foods/drinks, sugar has an important structural functionality in some foods. Reformulation of food/drinks is one way of reducing the glycemic effects, however another promising approach is by enriching them with alternative sugars that hinder sugar uptake. L-arabinose is a five-carbon sugar widely found in nature, for example in hemicellulose and pectin, that inhibits sucrase activity and it may be manufactured from sugar beets. Search was performed in two databases: Google Scholar and Scopus. In total 8 papers were included based on the criteria, 5 studies looked at acute effects – one-time exposure to an enriched food/drink - and 3 investigated longer term effects of L-arabinose enrichment. Almost all studies showed a beneficial effect on blood glucose, as well as a beneficial effect on insulin. No effects were observed on satiety, food intake or body weight. Importantly, no side effects were reported. Heterogeneity of the studies, poor design and reporting of the studies made further quantitative analyses impossible. Studies varied in the dose of L-arabinose, the dose of sucrose, type of product/matrix/nutrition composition and the population under study, i.e. healthy or diabetic population. L-arabinose enrichment of foods/drinks high in sucrose is a promising approach for lowering postprandial glycaemic responses. However, well-designed randomized clinical trials are needed to further explore the potential for enrichment of L-arabinose for sugar containing food applications.

P36 **Rats Exhibit Variability In Taste-Dependent Responses To Sucrose Octaacetate.**

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It has been well described in mice that taste responsivity to sucrose octaacetate (SOA) is variable, and depends on allelic variation at the *Soa* locus; unconditioned licking and nerve (chorda tympani and glossopharyngeal) responses are strongly suppressed in SOA taste-blind mice. We wished to explore potential variability in the taste response to SOA in rats. To do this, we trained rats to complete a modified forced choice task and asked them to discriminate between quinine and SOA. Multiple concentrations of each solution were tested simultaneously, so rats could not discriminate based on intensity of the stimuli. We found that on average, rats showed a weak ability to discriminate between quinine and SOA ($64.9 \pm 2.63\%$ correct, 50% = chance performance), but their individual ability to discriminate these solutions was variable (48-73%). Following this, we recorded unconditioned licking responses with these same rats to a range of SOA concentrations in a brief-access taste test. Again, rats showed variability in their avoidance of SOA, with some rats rejecting higher concentrations of SOA while others were relatively unaffected (varying from 4-54 licks at 3mM). Despite this, rats showed no significant correlation between discrimination and unconditioned licking ($r = 0.210$, $p = 0.404$), indicating that their ability to discriminate SOA from quinine was not related to their avoidance of the stimulus. Finally, we tested these rats in the brief-access taste test, using a range of sucralose concentrations. While animals did exhibit the previously described bimodal preference for sucralose, this was unrelated to their avoidance of SOA ($r = 0.021$, $p = 0.933$).

P37 **Acute Exposure To Blue Light At Night Impairs Glucose Tolerance, Alters Insulin Secretion And Increase Sugar Intake In A Diurnal Rodent**

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Nocturnal exposure to light containing short wavelength emissions (~450-500 nm) can disrupt the biological clock, alter sleep-wake cycles and induce metabolic changes. We reported that light at night (LAN) acutely impairs glucose tolerance in nocturnal rats. However, in nocturnal rodents, LAN coincides with their activity period, in contrast to artificial LAN exposure in humans. The aim of this study was to evaluate the acute effects of blue (λ= 490 ±20 nm) artificial light at night (bALAN) on glucose metabolism and food intake in diurnal Sudanian grass rats (*Arvicanthis ansorgei*) of both sexes, fed either regular chow or a free choice high-fat high sucrose diet. At Zeitgeber Time 14 (ZT14) a 1h pulse of bALAN was given and an oral glucose tolerance test (OGTT) was started at ZT15. One week later, a second light pulse was given and food intake was evaluated in both diet groups every 12h, the day before and the day after the light exposure. Finally, a week later a third light pulse was given and blood was sampled at ZT15 for glucose, insulin and corticosterone analyses. In chow-fed animals, the AUC of the OGTT was significantly higher in bALAN exposed animals of both sexes in comparison to dark controls. This was also observed in males, but not females fed the HFHS diet. bALAN induced an increase of sucrose intake in male *Arvicanthis* in the night of the light pulse. In chow and HFHS fed males, a significant decrease in plasma insulin concentrations was observed after bALAN exposure. In summary, exposure to bALAN causes glucose intolerance in diurnal rodents, with a stronger effect in males when they were fed high caloric diet. Moreover, one hour of bALAN was sufficient to trigger a higher intake of sugar and to cause a dampening in the insulin release in male grass rats.

P38 **Ethanol Intake In Male And Female Rats Categorized As Sucralose Avoiders Or Sucralose Preferers**

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Variability in taste responsivity influences food and fluid selection. Like humans, when presented a “sweet”-tasting solution, rats will increase intake in a concentration-dependent manner. When presented sucralose (an artificial sweetener) and water in a two-bottle test, as concentration increases, some rats drink more sucralose (sucralose preferers; SP) while some rats drink less sucralose (sucralose avoiders; SA). Individual differences in oral and reward signaling may contribute to variability in alcohol intake. Humans describe the taste of ethanol as having a bitter component. Innately, rodents and humans avoid bitter compounds yet when paired with postoral cues, ethanol can be learned to be preferred. Here, male and female rats categorized as SA or SP were presented 1, 2, 4, 6, 8, and 10% ethanol for daily 1-h tests. All groups decreased intake as ethanol concentrations increased with no significant SA/SP group differences. Next, 0.1 and 1.0 mg/kg naltrexone were administered (i.p) before presentations of 4 and 6% ethanol. At 0.1 mg/kg naltrexone, SA females drank significantly less 4% ethanol than SP females (p=0.005). In contrast, intake of 4% ethanol decreased similarly for SA and SP males following naltrexone administration. Intake of 6% ethanol decreased similarly for SA and SP following naltrexone administration. Taken together, these findings suggest the SA/SP phenotype does not predict ethanol responses in an intake test when both oral and postoral cues contribute. Reward cues that drive ethanol intake appear to be different for female, but not male SA/SP rats. Thus, the association of SA/SP status with ethanol responsivity may be partially attributed by differences in endogenous opioid signaling.

P39 **Do Thirst Mechanisms Determine The Anorexigenic Actions Of Cart?**

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Using our patented “Deductive Reasoning Strategy” we identified the orphan G protein-coupled receptor, Gpr160, to be a cognate receptor for cocaine- and amphetamine-regulated transcript peptide (CART). We employed several approaches to establish the physical association of CART and GPR160 and validated the specificity of a commercially available antibody for use in vivo (passive neutralization) and for staining purposes. Pretreatment (4^{th} ventricle) of male rats with this antibody prevented the anorexigenic effect of exogenous CART given also into the 4^{th} ventricle. Interestingly, similar administration of the antibody just prior to lights out resulted in increased water intake before any significant effect to increase food intake was observed. This suggests that the suppressive effect of endogenously produced CART, released from the vagus nerve upon initiation of a meal, may result in inhibition of not only food intake, but also water drinking. We seek now to determine if the two actions are related and possibly interdependent. Finally, we have localized Gpr160 expression to numerous brain sites known to be important in both feeding and drinking behaviors and seek using site-specific peptide and interfering RNA construct administrations to determine the areas relevant for these behaviors. Supported by NIH RO1 DK118340 to GLCY.

P40 **Fluid And Electrolyte Disturbances Mediated By Melanocortin-4 Receptor-Deficiency.**

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Melanocortin-4 receptor (Mc4r)-signalling has been extensively studied with regard to energy balance, however, the role of Mc4r ablation on fluid balance is unresolved. We found that basal water intake in rats lacking Mc4r (Mc4r-/-) was lower than in wildtype (Mc4r+/+) rats. Water intake was also lower in Mc4r-/- rats than Mc4r+/+ in response to fluid deprivation, hypovolemic challenge and peripheral angiotensin-converting enzyme inhibition. However, when administered hypertonic saline, Mc4r+/+ and Mc4r-/- rats had similarly increased fluid intake. Mc4r-/- rats had reduced CRH in the paraventricular nucleus of hypothalamus (PVN), heart rate, and renin expression in the kidney; suggesting a reduced sympathetic output from the PVN. Using Mc4r-/- mice, and Mc4r-/- mice with reinstatement of Mc4r in Sim1 neurons in the PVN, we found that following food and fluid

deprivation, Mc4r-/- mice drank significantly less water than Mc4r+/+ mice. Sim1-cre Mc4r mice drank the same as their cre controls, demonstrating that Mc4r in Sim1-expressing cells of the PVN are essential for normal sympathetic stimulation of RAS function. Overall, the data reveal a previously unreported role for the PVN Mc4r in fluid balance.

P41 **Neural Circuits Connecting Angiotensin Ii-Responsive Brain Areas With Structures Involved In Associative Learning**

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Recent studies provide evidence for a role of associative learning in the enhanced response observed after daily injections of angiotensin II (Ang-II). Specifically, the findings suggest that an observed increased drinking response after daily Ang-II involves a strengthening of the association between the stimulus (Ang-II) and the response (drinking). This effect appears to be mediated in part, by NMDA receptor activation, a critical component in associative learning, and there is a rich literature demonstrating the importance of the hippocampus in associative learning. Although the neural pathways that connect drinking-related structures to areas involved in associative learning are poorly understood, we hypothesized the existence of a relay between the median preoptic nucleus (MnPO), a critical area for the drinking response to Ang-II, and the hippocampus. To test this hypothesis, we made injections of a retrograde tracer (CTb) into the hippocampus and made MnPO injections of an adeno-associated virus (AAV2/10) that is transported anterogradely and expresses mCherry under the CMV promoter. Retrogradely labeled cell bodies and anterogradely labeled fibers were found in several brain areas, but the most striking overlap of the two was in the paraventricular nucleus of the thalamus (PVT). This finding is consistent with the well-studied role of the PVT in learning and memory processes, and offers a novel circuit by which Ang-II-related signals in the MnPO can access the hippocampus.

P42 **Thirst, Vasopressin Secretion And Reproduction Are Coordinated By The Activation Of Gpr173 By Phoenixin.**

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Using our patented “Deductive Reasoning Strategy” we identified the orphan G protein-coupled receptor, Gpr173, to be the cognate receptor for a novel hypothalamic peptide phoenixin (PNX) we discovered in 2014. We demonstrated PNX to exert multiple hypothalamic effects, some sexually dimorphic in nature. PNX binding to Gpr173 was demonstrated to be essential for normal ovarian cyclicity in rats, through interactions at the hypothalamic and pituitary levels. The localization of both peptide and receptor in PVN and SON suggested a role for PNX in vasopressin secretion, which we now have demonstrated to be physiologically relevant. We hypothesized that PNX may be an important factor controlling changes in fluid and electrolyte homeostasis that occur during the female life cycle. We have observed significant changes in receptor message during the female pubertal event, cyclic fluctuations in Gpr173 expression across the estrous cycle and, surprisingly, a physiologically relevant action of PNX to stimulate water drinking in the rat. This has led to a second hypothesis, that the paradoxical hypersecretion of AVP during the hypervolemic, hyponatremic state of pregnancy is a reflection of increased PNX activity. We will present evidence that PNX is a physiologically relevant regulator of AVP secretion and thirst, suggesting a novel explanation for the mechanisms underlying the volume loaded state of pregnancy and lactation.

P43 **Expression Of Angiotensin Type-1A And Type-2 Receptors In The Tongue And Taste Bud.**

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Mechanisms regulating gustatory detection of nutrients are important for understanding the etiology and treatment of hypertension and obesity. Angiotensin II (AngII) is a peptide hormone that is known to contribute to hypertension and obesity; however, its role in gustatory processes is largely unknown. The effects of Ang-II are exerted via its stimulation of angiotensin type-1a (AT1aR) or type-2 receptors (AT2R) and prior work has found that AT1aR is present on alpha-ENaC-expressing taste cells in the tongue and its stimulation alters salty and sweet taste sensitivity. Here, we further explore a role for Ang-II in gustation by evaluating the distribution of the AT1aR and AT2R on tongue and taste bud. Using three genetically-engineered reporter mouse lines, our studies combined *in situ* hybridization, immunohistochemistry, and the CUBIC tissue clearing method to evaluate expression of AT1aR and AT2R in the taste bud or tongue. Immunostaining of tongues from AT1aR-tdTomato mice confirmed expression of AT1aR in fungiform papillae taste receptor cells (TRCs), and revealed a high degree of co-localization with a marker for Type I TRCs (NTPDase). Using AT2R-GFP mice, we determined that although AT2R-expressing cells are localized to the tongue, there is limited expression of AT2R to the taste bud and a lack of co-localization with markers of TRCs. Finally, a dual AT1aR-tdTomato x AT2R-GFP reporter mouse line, confirmed no co-localization of AT1aR and AT2R within the tongue or taste bud and revealed that the spatial expression of AT2R increases from anterior to posterior. Collectively, these studies highlight the distribution of angiotensin receptors within the tongue and lay the groundwork for future experiments that will examine their functional relevance.

Saturday, July 13, 2019

8:30 - 10:30 AM	Progress
SYMPOSIUM 7: Ghrelin: don't call it a comeback!	

Chair(s): Suzanne Dickson and Alex Johnson

8:30 **Brain Ghrelin Receptor (Ghsr) Regulation Of Behaviour; Mood, Motivation, Metabolism And Memory**
ZANE ANDREWS
Biomedicine Discovery Institute, Monash University, Melbourne, Australia

9:00 **Ghrelin At The Intersection Between Stress, Metabolism And Resilience**
ALFONSO ABIZAID
Carleton University, Ottawa, ON, Canada

Ghrelin, a hormone associated with feeding and adiposity, is also one playing an important role in the adaptations required to meet the energetic demands posed by stressors. Indeed, ghrelin is secreted in response to acute and chronic stressors, and targets ghrelin receptors (GHSR) in hypothalamic and extrahypothalamic regions to mitigate the effects of chronic stress. Our work shows that ghrelin is secreted in response to chronic social defeat stress and that this increase in ghrelin is associated with increased caloric intake, and in metabolic changes that result in an adipogenic state. Moreover, chronic social defeat also results in increased expression of GHSR in the ventral tegmental area, a midbrain region that contains dopamine neurons that important for reward seeking behavior, and one also affected by chronic social defeat stress. Interestigly, mice treated chronically with GHSR receptor antagonists delivered into the VTA, or with targeted mutations to the GHSR gene show anxiety-like behaviors that are rescued in mice where the GHSR is rescued in the VTA. Finally, our work shows that ghrelin acts on the paraventricular nucleus of the hypothalamus to prevent chronic activation of the sympathetic nervous system and mice that are treated with GHSR receptor antagonists have chrinically elevated plasma levels of epinephrine and norepinephrine. In all, our data demonstrates that ghrelin plays an important allostatic role in the mechanisms that regulate sympathetic and hormonal responses to psychosocial stressors, and is an important factor in promoting resilience.

9:30 **A Ghrelin-Growth Hormone Stress Axis**
KI A. GOOSENS
Icahn School of Medicine at Mount Sinai, New York, NY, United States

The hypothalamus-pituitary-adrenal (HPA) axis is the canonical system for responding to stressors, with both adaptations and maladaptations following from its activation. However, there is not a clear relationship between the levels of these hormones and stress-associated mental illnesses such as post-traumatic stress disorder (PTSD), suggesting that hormones outside the HPA axis may drive some stress-related maladaptations. Recent findings show that ghrelin, a gastric peptide that crosses the blood-brain barrier, is elevated by stress. Here, I will present a series of experiments demonstrating an essential, novel, and HPA-independent role for a ghrelin-growth hormone axis in stress-related change in affective circuits. First, I will show that in unstressed rodents, endogenous peripheral acyl-ghrelin robustly inhibits fear memory consolidation through actions in the amygdala and, surprisingly, accounts for virtually all inter-individual variability in long-term fear memory strength. Thus, ghrelin is an endogenous inhibitor of fear memory which accounts for individual resilience or vulnerability to traumatic memories. In contrast, I will show that rodents exposed to chronic stress display chronically elevated acyl-ghrelin and that this promotes the overconsolidation of fear memories by inducing central ghrelin resistance, a novel form of metabolic resistance. Also, growth hormone, a downstream effector of ghrelin receptor activation, is increased in the amygdala by stress and virus-mediated overexpression in the amygdala of unstressed animals leads to excessive fear learning. These results suggest that a ghrelin-growth hormone stress axis mediates a novel branch of the stress response and highlight a previously unrecognized role for ghrelin in stress-associated maladaptation.

10:00 **The Endogenous Ghrelin Receptor Antagonist Leap2 Changes With Body Mass And Feeding In Humans And Mice.**
BHARATH K. MANI[1], NANCY PUZZIFERRI[2,3], JUAN RODRIGUEZ[1], SHERRI OSBORNE-LAWRENCE[1], NATHAN METZGER[1], ANTHONY P. GOLDSTONE[4,5,6], JEFFREY M. ZIGMAN[1,7,8]
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Sciences, Imperial College London, Hammersmith Hospital, London, United Kingdom, [6]Imperial Centre for Endocrinology, Imperial College Healthcare NHS Trust, St Mary's and Charing Cross Hospitals, London, United Kingdom, [7]Division of Endocrinology & Metabolism, Department of Internal Medicine, Dallas, TX, United States, [8]Department of Psychiatry, University of Texas Southwestern Medical Center, Dallas, TX, United States

LEAP2 (Liver Enriched Antimicrobial Peptide-2) has been newly characterized as a ghrelin receptor antagonist and inverse agonist. Here, we hypothesize that changes in plasma LEAP2 enhance ghrelin's metabolic actions during fasted conditions while facilitating ghrelin resistance in obese states. To test this hypothesis, we determined changes in plasma LEAP2 and acyl-ghrelin due to fasting, eating, obesity, bariatric surgery, glucose administration, and Type 1 diabetes mellitus, using human subjects and/or mice. Plasma LEAP2 positively correlated with BMI in humans and fat mass content in mice. Fasting lowered LEAP2 in humans with obesity and in lean mice. Oral glucose administration increased LEAP2 in fasted mice. These changes in LEAP2 were mostly opposite to those of acyl-ghrelin (except following bariatric surgery or in a Type 1 diabetes model), leading to robust increases in the plasma LEAP2:acyl-ghrelin ratio in conditions of obesity and robust falls in the LEAP2:acyl-ghrelin ratio during fasted states. These results suggest that plasma LEAP2 is physiologically regulated by metabolic status, with its levels increasing with body mass and blood glucose, and decreasing with fasting. These metabolically-regulated changes to plasma LEAP2 are opposite to those for acyl-ghrelin in lean subjects and subjects with obesity in both the fed and fasted states but not following bariatric surgery or in a mouse model of Type 1 diabetes. We predict that the plasma LEAP2:acyl-ghrelin ratio may be a key determinant modulating acyl-ghrelin activity in response to changes in body mass, feeding status, or blood glucose. We also propose that elevated plasma LEAP2 may confer ghrelin resistance during obese states, as would also be indicated by a higher plasma LEAP2:acyl-ghrelin ratio.

8:30 - 10:30 AM	Mission 1
ORAL SESSION 7: Eating Behavior and Obesity	

Chair(s): Bobby Cheon and Grace Shearrer

8:30 **Healthier Food Preference Following Roux-En-Y Gastric Bypass Surgery For Obesity, And Relationship With Weight Loss And Satiety Gut Hormones Pyy, Glp1 And Fgf19**

GHADAH ALDUBAIKHI[1], NAVPREET CHHINA[1], TASYA PARASTIKA[1], BEENISH ZAKI[1], NKECKI ONOKWAI [1], CAREL W LE ROUX[2], GRAHAM S FINLAYSON[3], ANTHONY P GOLDSTONE[1]

[1]Imperial College London, London, United Kingdom, [2]University College Dublin, Dublin, Ireland, [3]University of Leeds, Leeds, United Kingdom

Roux-en-Y gastric bypass (RYGB) surgery improves body weight, eating behaviour and appetite, in part via increases in gut hormones PYY, GLP-1 and FGF19. The Leeds Food Preference Questionnaire (LFPQ) assesses liking, wanting, and choice of different foods: low fat (LF), high fat (HF), savoury, sweet. Adults with obesity completed the LFPQ having fasted overnight, before and 14 weeks and 2y post-RYGB surgery. Plasma PYY, GLP-1, FGF19 concentrations were assayed before and after an *ad libitum*test meal (delta AUC (0-2h) adjusted for total kcal eaten). 14 adults (13 female, mean age 49y, BMI 45.9 kg/m2) completed follow-up at 14.9 weeks [range 11.0-17.4] post-RYGB (weight loss 21.8 kg [15.3-31.1]), and n=8 at 2 years. There was no significant time x fat x sweet interaction for any LFPQ variable. For explicit liking and wanting, a time x sweet interaction (P=0.03-0.01) was driven by decrease for sweet foods (both P< 0.001), and a time x fat interaction (P=0.006-0.004) by a decrease for HF foods (both P=0.001). Food choice, and implicit wanting (choice reaction time adjusted for choice frequency), switched towards savoury over sweet (both P=0.01), and LF over HF (both P=0.001), foods post-RYGB. Similar results were seen 2 years post-RYGB. After RYGB, post-prandial plasma PYY, GLP1 and FGF-19 increased by 3-6x (P=0.03-0.001, n=13). However, there were no significant correlations between changes in LFPQ variables and increases in gut hormones, nor weight loss at 14 weeks and 1 year post-RYGB. Food liking, wanting and choice moved away from foods high in fat and sugar after RYGB that was maintained for 2 years. However, inter-individual variations did not relate to differences in satiety gut hormones or weight loss. Analyses are also examining effects of lifestyle modification alone.

8:45 **Caloric Compensation, Appetite Control, And Eating In The Absence Of Hunger In Children At High Or Low Risk For Obesity**

TANJA VE KRAL [1], RENEE H MOORE [2], JESSE CHITTAMS[1], LAUREN O'MALLEY [1], ELIZABETH JONES [1], RYAN J QUINN [1], JENNIFER O FISHER [3]

[1]University of Pennsylvania, Philadelphia, PA, United States, [2]Emory University, Atlanta, GA, United States, [3]Temple University , Philadelphia, PA, United States

It is possible that obesogenic eating phenotypes manifest themselves *before* children develop obesity. We examined caloric compensation (%COMPX) and appetite in 212 normal-weight (NW) and obese (OB) children, ages 7 to 9, who were at high risk (HR) or low risk (LR) for obesity. Another aim was to assess if eating in the absence of hunger (EAH), which refers to eating when satiated in the presence of palatable energy-dense (ED) snacks, extends to healthier low ED snacks. In a crossover design, children ate breakfast, lunch, and dinner in the lab once a week for two weeks. 25 minutes before breakfast, children ate one of two compulsory preloads, which varied in ED (1.00 or 1.60 kcal/g). EAH was assessed after lunch and dinner when children received either low ED (fruit) or high ED (candy) snacks. At regular intervals, children's appetite sensations were measured and the satiety quotient (SQ) and 3-hr postprandial area under the curve (AUC) computed. There were no significant differences in %COMPX, SQ, or AUC among risk groups. SQs for Hunger and Prospective Consumption (PC) were higher and SQ for Fullness lower after consuming the low ED compared to the high ED preload ($p< 0.009$). The SQ for Desire and AUCs for Desire and PC predicted energy intake during the remainder of the day ($p< 0.03$). In both snack conditions, HR-OB children showed significantly greater EAH than LR-NW and HR-NW children ($p< 0.03$). Serving fruit rather than candy reduced energy intake, on average, by 60% (223 kcal) across groups. While we did not find that obesogenic eating phenotypes manifest themselves before children develop obesity, our findings do suggest that lowering foods' ED and substituting high ED snacks with fruit may help modify appetite sensations and moderate energy intake in all children.

9:00 **Obesity Causes Personality - Evidence From Twins**

UKU VAINIK[1,2], DANIEL BRILEY[3], LUCIA COLODRO-CONDE[4], ERIK MORTENSEN[5], KERRY JANG[6], JUKO ANDO[7], CHRISTIAN KANDLER[8], THORKILD I.A. SøRENSEN[9], ALAIN DAGHER[2], RENé MõTTUS[10,1]

[1]University of Tartu, Tartu, Estonia, [2]McGill University, Montreal, QC, Canada, [3] University of Illinois, Urbana-Champaign, IL, United States, [4]QIMR Berghofer Medical Research Institute,, Brisbane, Australia, [5]University of Copenhagen, Copenhagen, BC, Denmark, [6]University of British Columbia, Vancouver, Canada, [7]Keio University, Tokyo, Japan, [8] University of Bremen, Bremen, Germany, [9] University of Copenhagen, Copenhagen, Denmark, [10], University of Edinburgh, Edinburgh, United Kingdom

Obesity has associations with many personality traits. Causality in these associations is unclear, as randomised

control trials are impossible and longitudinal studies are rare. Here, we infer causality from cross-sectional twin data with direction-of-causation (DoC) models. In 4,578 twins from five countries (15% overweight, 5% obese), we studied relations between BMI and personality question risk score for BMI (QRS). For QRS, each participant's scores on 240 NEO PI-R questions were multiplied by the questions' meta-analytic association with BMI. These products were summed across questions to obtain a personal QRS, so a high QRS represents a higher personality-based risk for increased BMI. In DoC models, variance in QRS and BMI is separated into genetic (A), common environmental (C), and unique environmental components (E). DoC models assume that if outcome is causally explained by the phenotype, then the ACE components of the phenotype should be represented in the outcome proportional to the observed association. We assessed fit of four models: 1) a common factor causing BMI and QRS, 2) reciprocal causation, 3) QRS causing BMI, and 4) BMI causing QRS. We found that BMI was A = 74% (se = 1.3%) heritable, and QRS was A = 42% (se = 2.3%) heritable. Only E explained remaining variance. QRS and BMI correlated at r = .15 ($p < .001$). There was a genetic correlation (rg = .24, $p < .001$) but no environmental correlation. The best-fitting DoC model was nr 4), proposing that BMI causes QRS (lowest BIC, CFI = .923, RMSEA = .059, SRMR = .085). In summary, BMI may contribute to a range of behaviours, thoughts, and feelings. If replicated in other samples and with other causal inference methods, the results will have implications for therapy design and models of personality development.

9:15 **Eating Behaviours Modify The Associations Between Risk Factors In The First 1000 Days And Growth Outcomes At Age 6 Years**

A. FOGEL[1], K. MCCRICKERD[1], I.M. ARIS[2], Y.S. LEE[3,4], Y.S. CHONG[3,4], C.G. FORDE[1,5]

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Risk factors during the first 1000 days have been linked with increased obesity risk, and recent findings from our Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort have shown that having 4 or more risk factors is associated with an 11 fold increased risk of obesity by 4 years (Aris et al 2018). The association between early life risk and the development of child eating behaviours requires further investigation. Our study examined associations between cumulated risk factors in the first 1000 days, growth outcomes at 6 years and eating behaviours among GUSTO children. Six risk factors were considered including maternal and paternal pre-pregnancy BMI, excessive gestational weight gain, raised fasting glucose in pregnancy, short breastfeeding duration and early introduction of solid foods. Composite risk scores were computed based on number and the type of risk factors present and associated with a series of measured lunchtime eating behaviours including ideal and actual portion size, eating rate (g/min), and energy intake at lunch and during an eating in the absence of hunger task (kcal). Results showed that higher risk scores predicted higher BMI and larger whole-body adiposity, as well as larger self-served food portions, faster eating rates and larger energy intakes at lunch ($p< 0.05$). Importantly, the strength of associations between higher risk scores and higher BMI were moderated by eating behaviours such that there were positive associations between risk scores and growth outcomes only among children who selected larger food portions, ate faster, and consumed more energy ($p< 0.05$). These results highlight the important role of the identified child eating behaviours in the transition from early life obesity risk factors to the development overweight and obesity.

9:30 **Dysfunction Of The Orbitofrontal Cortex In Diet-Induced Obesity**

LINDSAY NAEF, LAUREN SEABROOK, COREY BAIMEL, STEPHANIE BORGLAND
University of Calgary, Calgary, AB, Canada

The orbitofrontal cortex (OFC) is involved in the cognitive control of reward processing. It keeps information online and updates behaviour based on changing reward contingencies. Human studies have demonstrated that obesity is associated with lower behavioural adaptation to reward devaluation. The goal of the present experiments was to test the hypothesis that OFC is impaired in an animal model of diet-induced obesity associated with altered reward devaluation. Mice with diet-induced obesity display deficits in reward devaluation. Furthermore, obese mice exhibit decreased inhibitory input onto pyramidal neurons of the lateral OFC measured with whole cell patch clamp electrophysiology. To determine if decreased inhibitory input to pyramidal neurons leads to impairment in reward devaluation in normal weight animals, we expressed an inhibitory Designer Receptor Exclusively Activated by Designer Drugs (DREADD) in VGAT ires cre mice. Inhibition of GABAergic inputs to the lateral OFC by clozapine N-oxide (CNO) administration impairs reward devaluation. Restoring OFC GABAergic tone with the GABA uptake blocker NNC-711 in obese mice restores reward devaluation. Together, these results demonstrate that obesity induces neuroadaptations in the lateral OFC to alter the processing of sucrose rewards, such that obese mice do not accurately update the reward value of rewards.

9:45 **(Nita Award Winner) Gut Microbiota Dysbiosis Is Sufficient To Alter Appetitive Feeding Behavior In Rats.**

JIYOUNG S. KIM[1], KEVIN C. WILLIAMS[2], REBECCA A. KIRKLAND[1], MADELYN CARLSON[3], KIMBERLY G. FREEMAN[4], JESSICA M. SMITH[2], PHILIP V. HOLMES[2], CLAIRE B. DE LA SERRE[1]

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The hedonic value of food is a key driver of intake and high fat (HF) feeding alters reward signaling. Gut-originating signals interact with reward pathways; GI infusion of fat induces dopamine (DA) release in the striatum, which is lost with HF consumption. Diet-driven microbiota dysbiosis is involved in the etiology of obesity, but a role for microbiota in modulating reward signaling has not been investigated. In this study, we aimed to determine if dysbiosis could alter striatum DA signaling. Germ-free Fisher rats were colonized with microbiota from low fat (LF, 13% fat) or HF fed (45% fat) rats and designated as convLF or convHF; LF and HF control groups were also included (n=8/group). 3 weeks post-colonization (PC) rats were fitted with a cannula targeting the ventral striatum (VS). Dialysates were collected during LF and HF food consumption for DA and DA metabolites (DOPAC) quantification. Progressive-ratio (PR) responding was used to assess the rats' motivation towards HF food 10 weeks PC. Rats were sacrificed 14 weeks PC, and tyrosine hydroxylase (TH) levels in the ventral and dorsal striatum (DS) were determined by ELISA. 16S Illumina sequencing confirmed that receivers and donors rats shared microbiota profiles. ConvHF rats consumed more food and gained significantly more weight than convLF rats. HF and convHF rats displayed similar significant changes in TH levels compared to LF and convLF rats with increased TH in the VS and decreased TH in the DS. Additionally, DOPAC levels were significantly elevated in HF and convHF rats in response to HF food. Finally, convHF rats displayed a lower breaking point in PR responding than convLF rats. Taken together, these data show that microbiota dysbiosis is sufficient to alter reward signaling in rats. NIDDK#1021RR581526

10:00 ***Associations Of Weight Status, Hedonics, And Reinforcing Value Of Food In Response To Snack Food Intake Among Adolescents***

AMANDA M ZIEGLER, TEGAN H MANSOURI, AMANDA K CRANDALL, JENNIFER L TEMPLE
SUNY University at Buffalo, Buffalo, NY, United States

Food hedonics, palatability, and reinforcing value (RRV) are independent drivers of eating behavior in adults, however these relationships are underexplored among adolescents. Our previous work showed that 2-weeks of repeated snack food consumption decreased liking of food, but increased RRV of food in adults with overweight and obesity. This increase was associated with greater weight gain over time. This study sought to understand the relationships among adolescent weight status, food hedonics, and change in RRV of high and low energy dense (HED and LED) foods, after 2 weeks of snack food monotony. We tested the hypothesis that increases in HED RRV after 2 weeks of intake are associated with greater zBMI at baseline and that the hedonic ratings and RRV will be dissociated in participants with higher zBMI in a large sample of adolescents. We categorized individuals as satiators (< RRV), stable (no change in RRV), or sensitizers (>RRV) based on changes in RRV after 2 weeks of intake. There were no differences in baseline hedonics or RRV of food by weight status. There were significant differences in the change in hedonic ratings of food over 2-weeks by sensitization group, with sensitizors showing a smaller decline in hedonic ratings over time compared with the other two groups. Changes in hedonic ratings were not related to zBMI while sensitization to HED, but not LED, food was associated with greater zBMI. The relationships between sensitization status and zBMI are similar to findings in adults, but the concordance between changes in hedonics and changes in RRV suggests that the adult behavioral phenotype has not yet developed. Future studies will examine the relationship between sensitization and weight change over time in this cohort.

10:15 **Greater Pre-Surgery Liking Of Combined Fat And Sugar Mixture Is Associated With Increased Twelve Month Weight Loss Following Rygb But Not Vsg.**

KIMBERLY R. SMITH[1], TIMOTHY H. MORAN[1], SUSAN CARNELL[1], KIMBERLEY E. STEELE[2]
[1]Department of Psychiatry and Behavioral Sciences, Johns Hopkins University, School of Medicine, Baltimore, MD, United States, [2]Department of Surgery, Johns Hopkins University, School of Medicine, Baltimore, MD, United States

While weight loss at one year following bariatric surgery often represents post-operative weight nadir and is a predictor of resolution of comorbidities, weight regain occurs in approximately 50% of all patients within 2 years. We previously showed that the bariatric procedures Roux-en-Y gastric bypass (RYGB) and vertical sleeve gastrectomy (VSG) resulted in similar significant weight loss 6 months post-surgery. Further, patients who preferred sugar-sweetened taste mixtures lost more weight at 6 months following RYGB but not following VSG. Here, patients returned for weight assessment 12 months post-surgery. Relative to their 6-month weight, 100% (23/23) of patients who underwent RYGB continued to lose weight, while 79% (22/28) of patients who underwent VSG continued to lose weight post-surgery. Overall, RYGB resulted in greater BMI point loss and percent total weight loss compared with VSG. We then divided the data from patients into 4 groups based on surgery and pre-surgical preference rating of a 10% fat and 10% added sugar, milk-based mixture on a 100-mm hedonic visual analog scale (VAS). Subjects who underwent RYGB and reported higher liking of the taste mixture (51-100 VAS rating; "preferrers") experienced greater BMI point loss and percent total weight loss at 12 months following surgery compared with RYGB recipients who reported lower liking (0-50 VAS rating; "non-preferrers") and all patients who underwent VSG regardless of liking rating.These data suggest a pre-surgical behavioral phenotype that may predict weight loss outcomes in patients who undergo bariatric surgery, specifically RYGB, and suggest a functional tool for clinical application in guiding patients toward a particular surgery type for optimal weight-loss success.

10:30 - 11:00 AM	Transit Zone
Coffee Break	

11:00 - 12:00 PM	Progress
MARS LECTURE 4	

Chair(s): Roger Adan

11:00 **The Brain Control Of Food Intake: Can An Old Dog Teach Us New Tricks?**
GILES YEO
University of Cambridge Metabolic Research Labs, Cambridge, United Kingdom

It is clear that the cause of obesity is a result of eating more than you burn. What is more complex to answer is why some people eat more than others? Over the past 20 years, insights from human and mouse genetics have illuminated multiple pathways within the brain that play a key role in the control of food intake. We now know that the brain leptin-melanocortin pathway is central to mammalian food intake control, with genetic disruption resulting in extreme obesity. These, however, remain rare, with the major burden of disease carried by those of us with 'common obesity'. In recent years, genome-wide association studies have revealed more than 100 different candidate genes linked to BMI, with most, including many components of the melanocortin pathway, acting in the CNS and influencing food intake. We have used a number of models to study the brain control of food intake, including drosophila and Labrador retrievers. We are also using single cell sequencing to study the expression profiles and heterogeneity of different hypothalamic cells in both mice and humans.

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

2:30 - 4:15 PM	Progress
AWARDS SESSION	

Chair(s): Michelle Lee, Tim Moran and Dana Small

2:30 **Introduction**

2:45 **Hoebel Prize For Creativity**
SUZANNE HIGGS
University of Birmingham

3:15 **Alan N. Epstein Research Award**
CARRIE FERRARIO
Assistant Professor of Pharmacology, The University of Michigan

3:45 **Distinguished Career Award**
MARGRIET WESTERTERP-PLANTENGA
NUTRIM, School for Nutrition and Translational Research In Metabolism, Faculty of Health sciences, Medicine, and Life sciences. Maastricht University Medical Centre

4:15 - 5:15 PM	Progress
SSIB Business Meeting	

7:00 - 12:00 AM	Polar
CLOSING BANQUET	