47th Annual Meeting of the Association for Chemoreception Sciences
April 23-26 2025
Bonita Springs, FL

Printable Program & Abstracts

Wednesday, April 23, 2025

10:00 - 11:55 AM	Calusa EFGH
Patient-Centered Discovery and Implementation Research in Chemosensory Health - Part 1	

Chair(s): Valentina Parma and Nancy Rawson

10:00 **Introduction: Addressing Gaps In Chemosensory Science: Bridging The Divide To Improve Patient Outcome**
Nancy Rawson

10:10 **Partnering For Progress: Laying The Foundation For Advancing Patient Partnerships In Chemosensory Research: Insights From A Pcori-Funded Patient Engagement Program**
Claire Murphy

10:30 **Experiences And Challenges In Partnering With Patients Throughout The Research To Translation Process - How To Best Collaborate With Researchers?**

Duncan Boak, Caroline Bigot , Pamela Silberman

11:00 **Opportunities And Gaps For Patient-Centered Research**
Roxana Chicas, Eric Holbrook, Danielle Reed

11:30 **Panel: Moving The Field Forward**

Moderator: Jonathan Overdevest & Jane Leland

Based on the experience discussed above, identify actions we can take to facilitate wider implementation of patient partnership across the chemosensory research community.

11:55 - 12:40 PM	Lunch On Own
Lunch On Own	

12:00 - 3:30 PM	Great Egret
Executive Committee Meeting (Invite Only)	

12:40 - 2:30 PM	Calusa EFGH
PATIENT-CENTERED DISCOVERY AND IMPLEMENTATION RESEARCH IN CHEMOSENSORY HEALTH – PART 2	

Chair(s): Valentina Parma and Nancy Rawson

12:40 **Introduction - What Do We Have And What Are We Missing? From Discovery To Implementation**

12:50 **Discovery - What Would New Techniques And Methods Unlock For The Treatment Of Smell And Taste Dysfunction?**
Brian Lin, Linda Barlow

1:20 **Clinical Perspective: Challenges And Opportunities In Developing And Delivering Treatments For Smell And Taste Dysfunction**
Jennifer Douglas, Sue Coldwell

1:50 **Regulatory, Dissemination & Implementation**
Patricia Lucas-Schnarre, Rick Geoffrion

2:07 **Patient Perspectives On Roadmap To Interventions**
Pamela Silberman, Duncan Boak, Caroline Bigot

Moderator: Jonathan Overdevest & Jane Leland

2:30 - 2:45 PM	Calusa Foyer
Coffee Break	

2:45 - 4:00 PM	Calusa EFGH
CONSENSUS ROUNDTABLE: ROADMAP TO IMPROVED DIAGNOSIS AND TREATMENT FOR CHEMOSENSORY DYSFUNCTION	

Insights from this discussion will contribute to a collaborative white paper, with contributing attendees recognized as co-authors

Chair(s): Valentina Parma and Nancy Rawson

2:45 **Introduction - Six Thinking Hats Methodology**
Nancy Rawson

2:50 **Discussion In Groups - Produce A Short, Medium And Long Term Action Item To Improve Diagnosis And Treatment Of Chemosensory Dysfunction**

3:45 **Analysis Of Action Items & Closing Remarks**

4:00 - 5:00 PM	Calusa Terrace
Diversity Fellowship Meet and Greet	

5:00 - 5:30 PM	Calusa EFGH
Welcome & Awards Ceremony	

5:30 - 6:30 PM	Calusa EFGH
Keynote Lecture	

5:30 **The Mind Of A Bee**
Lars Chittka
University of London

6:30 - 8:30 PM	Waterfall Pool Deck
Welcome Banquet (Ticket Required)	

Thursday, April 24, 2025

7:30 - 9:00 AM	Estero Foyer
Breakfast with Industry	

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Our purpose is to create what is essential for life, desirable for consumers, and more sustainable for the planet. Join us at our table to discover what diverse research careers are possible for industry scientists in a variety of research and product development roles in areas such as receptor biology, neuroscience, microbiome, psychophysics, materials science, chemistry, and technical product development.

Cargill
Cargill, a global leader in food and agriculture, is committed to providing food, ingredients, agricultural solutions, and industrial products to nourish the world in a safe, responsible, and sustainable way. Sitting at the heart of the supply chain, we partner with farmers and customers to source, make and deliver products that are vital for living.

Sensonics International
Sensonics International provides high-quality smell and taste tests for medical, scientific, and industrial use. Our Smell Identification Test™ (UPSIT®) is the world's most widely used olfactory test. We offer innovative electrogustometers, taste tests, and the Sensametrix® Smell Training System. Our products are globally distributed. Currently expanding and seeking qualified scientists to support our research program.

8:00 - 10:00 AM	Estero Ballroom
Poster Session I	

100 **Differential Effects Of Human *Apoliprotein* Alleles On The Mouse Olfactory Epithelium**

Timothy S McClintock[1], Abby Frazier[1], Gregory S Hawk[2], Lance A Johnson[1,3]
[1]Department of Physiology, University of Kentucky, Lexington, KY, United States, [2]Department of Statistics, University of Kentucky, Lexington, KY, United States, [3] Sanders Brown Center on Aging, University of Kentucky, Lexington, KY, United States

Alzheimer's disease (AD) is a progressive age-dependent disorder whose risk is determined by genetic factors. Better models for investigating early effects of highly penetrant risk factors such as *apolipoprotein E (APOE)* genotype are needed. To determine whether *APOE* genotype produces neuropathologies in an AD-susceptible neural system we compared effects of human *APOE-e2* (E2), human *APOE-e3* (E3), and *APOE-e4* (E4) alleles on the mouse olfactory epithelium. Just as in the brain where *Apoe* is expressed by astrocytes and microglia, sustentacular cells of the olfactory epithelium express *Apoe*. Comparison of E3 and E4 olfactory mucosae reveal only 121 differentially abundant mRNAs at age 6 months. Decreased abundance of mRNAs encoding oxidoreductases in E4 olfactory mucosae does not translate into differences in cellular respiration but olfactory mucosae in young adult E4 mice do show lower glucose uptake, characteristic of susceptibility to AD. Olfactory sensory neuron apoptosis does not differ at age 6 months but is greater in E4 mice at 10 months. At this age, differences in mRNA abundance are also greater and much more widespread, with > 750 differentially abundant mRNAs between each genotype. Bioinformatics analyses predict transcriptional regulation, ubiquitin ligase conjugation, and axon guidance are the largest phenotypic effects in E4 olfactory mucosae. Human *APOE* alleles begin to affect the phenotypes of mouse of olfactory epithelial cells, especially the sensory neurons, in early adulthood and these effects become more substantial by middle age. The olfactory epithelium and its olfactory sensory neurons are appropriate models in which to study the ability of human *APOE* alleles to modulate age-dependent effects associated with the progression of AD.

102 **Comprehensive Analysis Of Vomeronasal Receptor Isoforms In Mice**

Sachiko Haga-Yamanaka, Andrea Rocha, Ryan Kelso
University of California, Riverside, Riverside, CA, United States

Sensory signals detected by olfactory sensory organs are critical regulators of animal behavior. The vomeronasal organ (VNO) detects chemical cues from other animals and plays a pivotal role in intra- and inter-species interactions. These chemical cues are detected by vomeronasal receptors (VRs), which are exclusively expressed in the VNO. VR genes have been known to produce alternative splicing isoforms, including truncated open reading frames and variable untranslated region (UTR) lengths. However, the full repertoire, relative abundance, and biological significance of these isoforms remain poorly understood. In this study, to comprehensively analyze VR isoforms, we conducted long-read full-length RNA sequencing in the VNO of mice using PacBio platforms. Our data revealed that most VR genes produce multiple splicing isoforms, many of which encode

proteins of different lengths. Additionally, isoforms from a single receptor allele often vary in UTR length and sequence. Comparisons of VR gene isoforms suggest possible sex differences in their structures and relative abundances. Our findings suggest that VR genes generate diverse transcript isoforms, leading to receptor proteins with variations in length, sequence, and abundance. These variations, shaped by factors such as sex, may contribute to unique chemosensory perception in individual animals.

104 **From Nostrils To Olfactory Receptor: Temporal Precision Of Odor Stimuli During Sniffing**

Zhenxing Wu[1], John Scott[2], Kai Zhao[1]

[1]Department of Otolaryngology - Head & Neck Surgery, The Ohio State University, Columbus, OH, United States, [2]Department of Cell Biology, Emory University School of Medicine, Atlanta, GA, United States

The dynamics of airflow and odor transport during sniffing, which varies across species and depends on task, may play a pivotal role in modulating odorant stimuli and its temporal pattern. Here, we used a computational fluid dynamics (CFD) model to simulate the nasal aerodynamics and transport of various odorants with different solubilities in a rat and compared the results with the temporal neural activities measured by electro-olfactogram (EOG) under the same breathing frequencies (ranging from 0.5 Hz to 5 Hz). Our findings revealed a clear delay in the odor onset at the olfactory mucosa as compared to sniffing onset (from t=0.11±0.01s to 0.37±0.08s) that significantly correlated to the solubility of odorants, e.g., r=0.82, p<0.01 at 1Hz, r=0.77, p<0.05 at 2.5 Hz. Additionally, we observed a significant phase shift between the peak of odor absorption and the peak of sniffing (from 27% to 105% of the sniffing cycle) that significantly correlated with odorant solubility (e.g., r=0.84, p<0.01 at 1Hz; r=0.80, p<0.01 at 2.5 Hz) and increased with breathing frequencies. At the extreme, the odor sorption may peak at the exhalation phase or even at the inhalation phase of the next sniffing cycle. Furthermore, the peak absorption would continue to rise over several sniffing cycles (from 1 to 4 cycles) before reaching a high plateau. The EOG measurements closely matched the CFD simulation, validating our simulation results. This study highlights the importance of odor transport in preprocessing olfactory stimuli and that sniffing may function as an aerodynamic trap to accumulate (i.e., rising absorption peaks) and scramble odor stimuli (i.e., temporal shift) depending on odor solubility and sniffing frequencies, with key implications for temporal precision, olfactory coding, and sensory adaptation.

106 **A Phylogenetic Upgrade: Improved Accuracy Of Phylogenetic Classification Of Human Odorant Receptors**

Selma Valling Lauritsen, Vandana Kaushal, Sylvester Holt
University of Copenhagen, Frederiksberg, Denmark

The current classification of odorant receptors (ORs) is based on phylogenetic analyses conducted during the initial sequencing of the human genome. Since then, significant advancements in phylogenetic methods, computational power, and genome sequencing technologies have emerged. In this study, we performed a maximum likelihood phylogenetic analysis of 404 functionally expressed odorant receptors using IQ-TREE. Our results show that using T-Coffee for alignment, with profiles derived from transmembrane proteins, produced a higher quality phylogenetic tree compared to conventional alignment tools. The optimal model fit was achieved with a Jones-Taylor-Thornton (JTT) matrix, incorporating 8 γ-distributed rate categories and dataset-specific amino acid frequencies, based on AIC/BIC model selection criteria. Both Ultrafast Bootstrap and Approximate Likelihood Ratio Test (aLRT) methods significantly improved the reliability of the inferred receptor relationships. However, support for inner nodes was generally lower, especially with conventional bootstrapping, indicating that these nodes have a weak phylogenetic signal, possibly aggravated by the limitations of resampling methods. While our findings showed similarities with the existing phylogenetic classification, we also identified discrepancies, including several ORs that had been incorrectly classified, highlighting the enhanced accuracy of our approach. We are currently investigating the functional relationships of these clades with key odorants, aiming to better understand the functional diversity within this receptor family.

108 **Predicting Olfactory Receptor Activity Using Nanomechanical Sensors And Machine Learning**

Noriaki Ota[1], Yusuke Ihara[1], Kosuke Minami[2], Ryo Tamura[3], Genki Yoshikawa[2,4], Chiori Ijichi[1]

[1]Institute of Food Sciences and Technologies, Food Products Division, Ajinomoto Co., Inc., Kawasaki, Japan, [2]Research Center for Macromolecules and Biomaterials, National Institute for Materials Science (NIMS), Tsukuba, Japan, [3]Center for Basic Research on Materials, National Institute for Materials Science (NIMS), Tsukuba, Japan, [4]Graduate School of Pure and Applied Science, University of Tsukuba, Tsukuba, Japan

Humans perceive billions of odors through ~400 olfactory receptors (ORs). Since odor information is thought to be condensed into the activity of 400 ORs, obtaining the ORs activity profile for each scent is important for understanding, digitizing, and utilizing the sense of smell. We have obtained the OR activity profiles by a cell-based assay for ~3000 odorants and foods. However, there are several drawbacks to collecting data using cellular assays: measurements may not be possible due to cytotoxicity, on-site measurements are difficult to perform, and the process is time-consuming. Therefore, we worked on developing an algorithm to predict ORs activity without cell-based assays by combining nanomechanical sensors and machine learning methods. For the nanomechanical sensor, we used “Membrane-type Surface stress Sensor (MSS)", which is characterized by high sensitivity, high selectivity, and fast response. In this study, we used an MSS array with 12 different receptor layers to acquire 12 different signals in one measurement. We acquired signal data from about 300 odorants, for which ORs activity profiles had already been obtained. We then extracted features from the acquired signal data, created regression models to predict activity values for 10 representative ORs, and compared the prediction accuracy for each. The results showed that prediction accuracy could be improved by optimizing the selection of receptor layer signals data used as features. The model with the highest prediction accuracy was developed using

only three receptor layer signals data and predicted the activity of OR5K1 with a correlation coefficient (r) of about 0.733 in cross-validation. In this poster, we will report these results and discuss the relationship between receptor layers and OR activity prediction.

110 **Mammalian Chemosensory Bile Acid Detection Supports Gut Microbiome Evaluation**

Varun Haran[1], Mari Morimoto[1,2], Leena S.F. Rouyer[1], Julian P. Meeks[1]

[1]University of Rochester, Rochester, NY, United States, [2]City College of New York, New York, NY, United States

The rodent accessory olfactory system (AOS) plays a key role in detecting environmental chemosignals and guiding social and survival-oriented behaviors. Bile acids found in mouse feces act as AOS chemosensory ligands, activating vomeronasal sensory neurons (VSNs) and potentially serving as mammalian pheromones and kairomones. However, only a small number of molecules in this class of AOS ligands have been studied to date.

Using live volumetric Ca^{2+} imaging, we screened naturally occurring bile acids for their ability to activate peripheral vomeronasal sensory neurons (VSNs). We found that taurine-conjugated bile acids (tauro-BAs), including taurine-conjugates of cholic acid, deoxycholic acid, lithocholic acid, and chenodeoxycholic acid (TCA, TDCA, TLCA, TCDCA, respectively), activate larger populations of VSNs at sub-micromolar concentrations than their unconjugated and glycine-conjugated counterparts. Tauro-BAs were not detected in conventional mouse fecal extracts, but they were present in germ-free mouse feces extracts. VSN Ca^{2+} imaging confirmed that the tauro-BA ligands identified in germ-free mouse feces activated a large proportion of germ-free feces-responsive VSNs. Importantly, germ-free and conventional mouse fecal extracts activated almost exclusively non-overlapping populations of VSNs. To investigate the impact of tauro-BAs on behavior, we studied TDCA, which displayed particularly strong potency in Ca^{2+} imaging experiments. Fecal extracts spiked with TDCA acted as an aversive stimulus in both non-social and social behavior contexts. These studies establish that the gut microbiome plays an essential role in the secretion of social chemosignals and that VSN detection of taurine-conjugated bile acids supports gut microbiome evaluation.

112 **Novel 3D Shape And Pharmacophore Molecular Representation Of Odorants For Predicting Olfactory Receptor Activity And Odor Descriptor**

Yusuke Ihara[1], Chiori Ijichi[1], Takatsugu Hirokawa[2,3]

[1]Institute of Food Sciences and Technologies, Food Products Division, Ajinomoto Co., Inc., Kawasaki, Japan, [2]Division of Biomedical Science, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan, [3]Transborder Medical Research Center, University of Tsukuba, Tsukuba, Japan

Humans perceive billions of odors through the activity of 400 types of olfactory receptors (ORs). Elucidating this many-to-many combinatorial coding is crucial for digitizing olfaction. We have obtained comprehensive activity profiles of human ORs for approximately 3000 odorants using a cell-based assay system and constructed a database, Olfaction DB, which correlates these profiles with molecular structures and odor descriptors.
In this study, we analyzed the relationship between the molecular structures of odorants and OR activity or odor descriptors. Recent studies have predicted odor descriptors and OR activity from the molecular structures of odorants using machine learning technologies, including state-of-the-art graph neural networks. However, these methods did not consider the possibility that each odorant can take multiple conformations. Therefore, we have developed a novel molecular representation method that considers multiple conformations of odorants. This method assumes that a single odorant might take different conformations when activating different ORs, and that multiple odorants might take similar conformations when activating a common OR. Using this method, we generated 941-dimensional fingerprints for 941 diverse odorant components. The results of dimensional reduction and mapping of the odorants in a 3D space showed that molecular features such as functional groups and molecular sizes were reflected in the spatial arrangement. Furthermore, by visualizing the distribution of the activity values of OR5K1, OR4S2, and OR10G4, as well as the relevant odor descriptors, it was found that clusters were formed in characteristic positions depending on ORs and descriptors. These results suggest the potential for precise OR activity and odor quality prediction using this method.

114 **The Role Of The Complement System In Regulating The Stimulation-Dependent Neurogenesis Of Specific Olfactory Sensory Neuron Subtypes In Mice**

Alexa J. Asson, Madeline Smith, Karlin E. Rufenacht, Kawsar Hossain, Rebecca O. Rourke, Stephen W. Santoro
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Of the roughly 1200 olfactory sensory neuron (OSN) subtypes in the mouse olfactory epithelium (as defined by odorant receptor identity), a fraction has been found to undergo accelerated birth rates in the presence of odor stimulation compared to the absence. These findings challenge the established model that OSN neurogenesis is entirely stochastic with respect to subtype. We hypothesize that mature OSNs of this fraction of subtypes possess the unique ability to signal to proximate neuronal progenitors and thereby promote their proliferation in the presence of specific olfactory stimuli. To test this, scRNA-seq was used to compare the transcriptomes of OSN subtypes known to undergo stimulation dependent neurogenesis to those of random subtypes, revealing *Cd55*, a gene encoding a central inhibitor of the complement system, as one of a small number of genes selectively enriched in stimulation-dependent subtypes. Based on these findings, we hypothesized that CD55 plays a role in regulating stimulation-dependent OSN neurogenesis. To test this, we generated a mouse in which *Cd55* is knocked out specifically in neurons. Utilizing scRNA-seq and a combination of EdU-birthdating and RNA fluorescent in situ hybridization, we have found preliminary evidence that the birth rates of *Cd55*-expressing

OSN subtypes are accelerated by stimulation, that the effects of odor stimulation are attenuated in *Cd55*-knockout mice compared to controls, and that the overall rate of OSN neurogenesis is increased in *Cd55*-knockout mice. Taken together, our findings support a model in which the selective expression of CD55 by OSNs of a fraction of subtypes inhibits the activation of complement in their proximity and thereby selectively reduces the neurogenesis rates of specific subtypes in the absence of odor stimulation.

116 **The Sensory Organization That Drives Mosquito Host Detection**

Yifan Wang[1], Wesley Alford[1], Sheikh Kamran[1], Meg Younger[1,2]
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The increased prevalence of mosquito-borne disease is a major and public health issue. The best strategy to prevent the spread of mosquito-borne disease is to avoid their bites. Mosquitoes rely heavily on odor, carbon dioxide, and other chemosensory cues, which they detect through chemosensory receptors in their antennae, maxillary palps, and other sensory tissues. Mapping chemosensory receptor distribution in mosquito sensory tissue is an important step towards understanding the mechanisms that mosquitoes use to find humans. To study mosquito chemosensory systems, it is essential to generate a complete map of the receptors. To this end I am creatin receptor-to-neuron maps in mosquito antennae through spatial transcriptomics using the Xenium platform from 10x Genomics. I have designed a 300-gene panel for use with mosquito antennae. I find that I can detect the location of these chemoreceptor transcripts in segments of the antenna that are cryosectioned and that the transcripts I detect are consistent with both bulk and single nucleus RNA sequencing data. Moving forward, I will transform this data into a 3D map that will illustrate the distribution of receptors in cells along the antenna, and illustrate their relationship to landmarks in the tissue. This will establish a methodology for spatial transcriptomics and will generate essential receptor-to-neuron maps needed to study chemosensation in mosquitoes and other insects. These results will guide future work, to determine if there changes in receptor expression and distribution occur between different mosquito behavioral states and sexes. By determining the localization and changes of chemosensory receptors, we can enhance our understanding of the molecular mechanisms that underly the detection of humans by mosquitoes.

118 **Activity-Dependent Gene Regulation In Olfactory Sensory Neurons**

Joshua Danoff, Kevin Monahan
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Olfactory sensory neurons (OSNs) adapt to odor environments by dampening their response to abundant odorants and heightening their response to rare odorants. Neuronal adaptation requires transcriptional changes that ultimately tune the activity of each OSN to its environment, but the gene regulatory mechanisms enabling these transcriptional changes are unknown. Using ATAC-seq and scRNA-seq, we investigate how gene regulation and transcriptional responses to new environments enable this adaptation. First, we find abundant differential chromatin accessibility among OSNs that are highly active compared to those that are not active. Activity-open peaks are enriched for known transcription factors in OSNs, including Lhx2 and Ebf, and the neuronal activity-dependent transcription factor Nfat. Gene ontology analysis indicates that activity-open peaks are associated with genes involved in synaptic transmission and olfactory perception. Using a paradigm where mice are exposed to new odor environments, we then examine the role of the chromatin organizer cohesin in rapid adaptation of OSNs to new environments. scRNA-seq of olfactory sensory neurons shows that cohesin (*Rad21*) knockout impacts the ability of OSNs to adapt to new environments in an olfactory receptor (Olfr) dependent manner. Some OSN subtypes, expressing a specific Olfr, are unable to adapt to new odor environments without cohesin expression, while other OSN subtypes are not impacted by cohesin knockout. These results demonstrate the involvement of chromatin organization in regulating activity-dependent transcriptional adaptations in OSNs. Further, they also identify molecular targets of olfactory neuronal activation by odors and have implications for understanding activity-dependent transcription in neurons generally.

120 **zOna Pellucida Like Domain Containing 2 Mediates Stimulation-Dependent Neurogenesis Of Specific Olfactory Sensory Neuron Subtypes In Mice**

Karlin E Rufenacht, Alexa J Asson, Kawsar Hossain, Amanda Stenzel, Madeline Smith, Stephen W Santoro
Department of Pediatrics, Section of Developmental Biology, University of Colorado Anschutz Medical Campus , Aurora, CO, United States

Neurogenesis persists throughout life in the mammalian olfactory epithelium. In mice, differentiating olfactory sensory neuron precursors select for expression a single olfactory receptor gene, out of ~1200 possibilities, which determines the mature neuron's subtype. Our lab has found that odor stimulation can accelerate the birthrates of specific neuron subtypes, which challenges the established model that neurogenesis within the olfactory epithelium is stochastic with respect to subtype. To explain these findings, we hypothesize that upon stimulation, neurons of some subtypes have a special capacity to signal to progenitors to promote the birth of neurons of the same subtypes. In support of this, scRNA-seq analyses identified a few genes that are selectively expressed by neuron subtypes whose birthrates are accelerated by stimulation, including Zona pellucida like domain containing 2 (*Zpld2*), which is predicted to encode an extracellular membrane protein with potential involvement in neutrophil migration. To test whether *Zpld2* is involved in a signaling pathway that mediates stimulation-dependent neurogenesis, we generated a *Zpld2*-null mouse. Using scRNA-seq and a combination of EdU-birthdating and RNA-FISH, we have found preliminary evidence that *Zpld2*-expressing neuron subtypes undergo stimulation-dependent neurogenesis and that this phenomenon is attenuated in *Zpld2*-null mice compared to controls. Additionally, RNA-seq-based analyses have revealed a down-regulation of genes involved in neurogenesis and an up-regulation of genes involved in immune function in *Zpld2*-null epithelia. These

findings support a model in which, upon odor stimulation, neurons that express *Zpld2* signal to progenitors, possibly *via* neutrophils, to promote the neurogenesis of specific neuron subtypes.

122 **Unveiling The Molecular Mechanisms Of Odorant Receptors&Rsquo; Antagonism**

Mona A. Marie[1], Madison Herrboldt[6], Matt Wachowiak[6], Hiroaki Matsunami[2,3,4,5]

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Olfaction enables organisms to detect and differentiate an immense diversity of chemical compounds, with vertebrates relying on a vast repertoire of odorant receptors (ORs) to mediate this chemosensory perception. Our study fills a critical gap in understanding how odorant mixtures interact at the molecular and biological levels, revealing a conserved mechanism of competitive antagonism among Class I ORs. By using human OR51E2 and mouse Or52h2 as Class I receptor models, we demonstrate that longer-chain carboxylic acids antagonize the binding of short-chain acids within the limited volume of the OR binding cavity, a finding corroborated by functional analyses. Moreover, in vivo experiments using two-photon calcium imaging in awake head-fixed mice tagged with OMP-Cre; GCaMP8f; IRES-Or52h2-olfactory sensory neurons (OSNs) confirmed this competitive antagonism, with reduced calcium responses observed in the presence of agonist-antagonist mixtures. Our efforts in delineating odorant mixtures interactions also extended to Class II ORs, through identifying novel antagonists for this class of ORs, in our in vitro pipeline. Leveraging the lab's recently crystallized atomic level engineered receptor 1, structure (ConsOR1), we are able to computationally model native receptors in this class and show their molecular mechanism of antagonism. These findings provide a foundational understanding of how ORs process complex odorant mixtures, bridging molecular interactions with neural encoding in the olfactory system. Deciphering these mechanisms is a crucial step toward unraveling the principles governing olfactory perception, which has broad implications for sensory biology, odorant-based therapeutics, and the design of artificial olfactory systems.

124 **Evaluating Epithelial Microenvironment Effects On Olfaction: Anatomical, Metagenomic, And Functional Distinctions Between Olfactory And Respiratory Epithelia**

Pia LaPorte[1], Ludmila Globa[1], Oleg Pustovyy[1], Melissa Singletary[1,2]

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The microenvironment of most mucosal sites in mammalian tissue demonstrates an integral relationship between epithelial morphology, immunological balance, and overall function. To evaluate this relationship in olfactory epithelia, this work employs a combination of histological, metagenomic, and electrophysiological methods in the rat model. Isolated tissue from the nasal septa were prepared for microanatomical and functional analyses of olfactory epithelium (OE), respiratory epithelium (RE), and turbinates of the ethmoidal labyrinth. For comparative histological and immunohistochemical evaluation, Bouin's-preserved and paraffin-embedded sections were stained with H&E and PAS or immunologically tagged with OMP and GAP43 antibodies. Differential epithelial thickness and composition of cellular targets, including mature olfactory neurons, axon processes, and glandular structures, were observed between the OE and RE. Preliminary metagenomic work utilized shotgun sequencing to a minimum of 165M Illumina reads to evaluate the regional diversity and abundance of microbial taxa, revealing observable differences in OE and RE microenvironments. These structural and microbial distinctions were supported by functional analysis using the Electroolfactogram (EOG), where odor-evoked responses were recorded in the neuronal OE but not detectable in RE. Together, these results indicate that structure and microbial composition influence olfactory epithelial function. Further analyses of microbial diversity, antibiotic effects, and immunological responses are needed to fully elucidate the relationship between microbial community inhabitants and olfactory function across species.

126 **Characterizing The Sensorimotor Transformation In *Drosophila* Olfactory System In Response To Naturalistic Stimuli**

Samuel P Wechsler, Vikas Bhandawat
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Odors modulate locomotion in diverse ways, changing based on concentration, exposure duration and identity. The volatility and transience of odors make them hard to control, making it a challenge to study sensorimotor transformations. Using a circular arena with a vacuum-pulled central odor zone, we precisely controlled odor delivery to flies while describing behavior (Jung et al., 2015). To characterize the transformation between olfactory receptor neuron (ORN) activity and behavior, we replace the odor zone with a fixed-intensity light zone to optogenetically replicate the fly's sensory experience during behavior in an electrophysiological rig. Using this framework, we previously obtained the relationship between a group of ORNs activated by a strong attractant, apple cider vinegar and the resulting locomotor changes (Tao et al., 2024). Here, we apply the same experimental approach to investigate how a repellant ORN, Or7a, affects fly locomotion. Furthermore, we assess the role of the second-order projection neuron (PN) downstream of Or7a. These experiments utilize dual binary expression to simultaneously activate ORNs while inactivating or performing in-vivo whole-cell patch clamp recordings from PNs. We find that Or7a ORN activation produces repellant behavior that is surprisingly exacerbated with the PN signal removal. Our work looks to further understand how fly behavior is affected by this repellant

glomerulus' activation and the role PNs play in influencing these ORN-mediated locomotor changes. Our data provides new insights into the nature of sensorimotor transformations in the context of naturalistic odor stimulus by providing a comparative description of behavioral changes for a motor program that is independent from the previously described strong attractant-influenced behavior.

128 **Decoding The Olfactory Bulb Glomerular Map: Linking Odorant Receptor Identity To Odor Responses And Circuit Logic In The Mouse Olfactory System**

Zarmeena Dawood[1,3], Cristian Soitu [1], Alex Becalick[2], Walter G. Bast[1], Diego E. Hernandez[1], Kira Schoenberg[1], Petr Znamenskiy[2], Anthony M. Zador[1], Alexei Koulakov[1], Dinu F. Albeanu[1]
[1]Cold Spring Harbor Laboratory , Cold Spring Harbor, NY, United States, [2]Francis Crick Institute, London, United Kingdom, [3]Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY, United States

Odor perception begins with odorants binding odorant receptors (ORs) on olfactory sensory neurons (OSNs) in the nasal epithelium. OSN axons project to the olfactory bulb (OB), forming a stereotypic layout of glomeruli sorted by OR type. Odor information represented as spatial-temporal activations of glomeruli is then relayed by mitral and tufted cells (MTCs) to several brain regions, including the olfactory cortex. To date, we lack a clear understanding of what odorant properties drive percepts, and how these properties are represented in brain activity. A key difficulty lies in linking OR identities to their responses *in situ*, and determining how odor information is broadcast across the brain. We are pursuing DNA barcoding strategies to: 1) discover glomerular maps, i.e. identities of ORs projecting to most glomeruli (~3,000/OB hemisphere), 2) establish the relationship between the OR identity of ~250 glomeruli on the OB dorsal surface and large sets of odorants using Ca imaging, 3) develop machine learning algorithms to infer odorant-OR binding based on predicted OR 3D structure by using the measured functional data for training, and 4) determine the logic of olfactory circuits via DNA-barcoding connectivity mapping. We employed BARseq2, a high-throughput *in situ* sequencing method, to map OR distributions at sub-glomerular resolution in 20 μm OB slices. We designed ~8,500 padlock probes targeting all ~1,100 mouse OR genes and detected clear transcript clusters for 506 ORs *in situ* in two animals. Spatial analysis confirmed a dorsal bias for class I ORs and broader distribution of class II ORs. In parallel, we used barcoded Sindbis viruses to infect ~3,000 MTCs and trace their input glomeruli. Together, these approaches reveal how OR identity shapes OB outputs and underpins odor-driven behaviors.

130 **In Situ Hybridization Analysis For The Expression Of Olfactory Receptors In The Olfactory Organ Of Red-Bellied Short-Necked Turtle, *Emydura Subglobosa***

Shoko Nakamuta, Takuya Yokoyama, Yoshio Yamamoto, Nobuaki Nakamuta
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Turtle olfactory organ consists of upper (UCE) and lower chamber epithelium (LCE). The UCE, equipped with associated glands, and the LCE, devoid of glands, line the dorsal and ventral portion of nasal cavity, respectively. Generally, ciliated olfactory receptor neurons (ORNs) express odorant receptors (ORs) and microvillous ORNs express vomeronasal receptors in vertebrates. However, although UCE contains ciliated ORNs and LCE contains microvillous ORNs in many turtles, most ORNs express ORs regardless of whether they are ciliated or microvillous. To date, studies on turtle olfactory receptor expression are limited to hidden-necked turtles. Thus, a side-necked turtle, *Emydura subglobosa*, was examined to clarify the origin of LCE containing OR-expressing microvillous ORNs. In *E. subglobosa*, most ORNs expressed GNAL and CNGA2, suggesting the expression of ORs or trace amine-associated receptors (TAARs). Among ORs, class I ORs were mainly expressed in the LCE, while class II ORs in the UCE. In addition, all TAARs except TAAR1, including TAAR2, 4, 5, 7, and 9, were mainly expressed in the LCE. Present results suggest that most ORNs in both UCE and LCE of side-necked turtle express ORs, as in hidden-necked turtles. The olfactory organ containing OR-expressing ciliated ORNs in both UCE and LCE, as in side-necked turtle, has been demonstrated in soft-shelled turtles among hidden-necked turtles. Possibly, LCE in the common ancestor of turtles might have contained OR-expressing ciliated ORNs and, after the divergence of soft-shelled turtles, ORNs in the LCE of other hidden-necked turtles might have changed from ciliated to microvillous, leaving the expression of olfactory receptors unchanged.

132 **Ca2+-Activated Ion Channels Exert Opposite Effects In Different Signalling Compartments Of Vomeronasal Sensory Neurons**

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The mammalian accessory olfactory system regulates innate social and sexual behaviors. The chemical cues activating the system are detected by the vomeronasal organ (VNO) and processed in the accessory olfactory bulb (AOB). In the periphery, stimulation of vomeronasal sensory neurons (VSNs) at their microvillous dendritic knobs triggers a local signal transduction and amplification cascade. This signal is then transformed into action potential (AP) discharge at the soma. Both, signal transduction and information transfer via action potentials, involve local Ca^{2+} elevations in the knob and soma, respectively. Here, we revisit the still controversial functions of Ca^{2+}-activated ion channels in both VSN compartments. Using local Ca^{2+} uncaging during single-cell electrophysiological recordings in acute mouse VNO slices, we demonstrate that Ca^{2+}-activated ion channels exert opposite functions during primary transduction versus action potential firing. An increase of Ca^{2+} in the knob drives an excitatory inward current, while Ca^{2+} elevations in the soma primarily activate hyperpolarizing outward currents that silence VSNs. A substantial fraction of the latter current is mediated by SK and / or BK channels. Notably, SK channel activity strongly affects VSN firing. Together, our study reveals a diverse

composition of Ca^{2+}-activated currents in VSN somata and uncovers an unexpected role of SK channels in controlling AP discharge and thus in information transfer from the VNO to the AOB.

134 **Inhales And Exhales Are Characterized By Alternating Rhythmic Dominance Of Sympathetic And Parasympathetic Neuromodulators In The Human Olfactory Epithelium**

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Nasal breathing provides the olfactory system with a rhythmic, alternating sampling of external and internal environments. Inhales sample the external environment, and exhales sample the internal environment. These two sampling states are likely optimized through different sensory neuron response profiles, as the information obtained through them has different meanings, thus requiring different actions. For example, olfactory information received during inhales may require faster, more vigilant responses to potential environmental threats compared to olfactory information received during exhales, which may benefit from slower, broader responses, e.g. allowing appreciation of complex flavors. How might the olfactory system meet the need to dynamically optimize odor responses? One possibility is through rhythmic breathing-linked neuromodulation of olfactory sensory neurons (OSNs) consisting of alternating sympathetic (inhale, vigilance) and parasympathetic (exhale, relaxation) modulation. Indeed, rodent work has shown that sympathetic modulation of OSNs amplifies responses to strong odors, whereas parasympathetic modulation broadens responses to many odorants. Here, we hypothesized that natural nasal breathing would be accompanied by alternating rhythmic dominance of sympathetic and parasympathetic neuromodulators in the human olfactory epithelium. We used electrochemical methods to record sub-second changes in norepinephrine and serotonin concentrations in the human olfactory mucosa during natural nasal breathing and found that norepinephrine peaks during inhales, whereas serotonin peaks during exhales. These findings suggest that inhales and exhales result in alternating olfactory sampling states with distinct OSN signaling profiles.

136 **Evolution And Functional Characterization Of Olfactory Receptors In Birds**

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Birds are the most speciose class of terrestrial vertebrates, inhabiting nearly all land environments and with diverse social structures and foraging strategies, yet were long thought to make limited use of olfactory signals. Recent behavioral work in birds has shown important roles for olfaction in foraging and species recognition, among other behaviors. Contributing to this surge of interest in avian olfaction, our recent work has shown that birds have hundreds more OR genes in their genomes than previously realized. We have examined the genomic OR repertoire of over 120 high quality long-read bird genomes spanning the avian phylogeny, revealing between 50 and 3,750 intact ORs in all species surveyed. To discern the functional roles of ORs, we measured OR mRNA expression levels in the olfactory epithelium of four bird species and found that the majority of the bird OR genomic repertoire is expressed in tissue relevant to smell. With in situ hybridization we show that bird ORs are localized to the olfactory sensory neurons. To confirm the ability of bird ORs to detect odors, we expressed chicken ORs in mammalian cell culture, exposed ORs with multiple odors, and measured OR activation in response to each odor. We found that chicken ORs respond to several types of pyrazines, a group of chemicals that are found in the scent of green peppers. Together, these results show that bird ORs are diverse, evolve dynamically, are expressed in the olfactory epithelium, and are capable of functionally detecting odors. This work provides the foundation for future functional characterization of bird ORs across a variety of bird species.

138 **Rapid Antiviral Response And Suppressed Activity-Dependent Gene Expression In Olfactory Sensory Neurons Of Sars-Cov-2-Infected Olfactory Epithelium**

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Olfactory loss is a common symptom in COVID-19 patients. SARS-CoV-2 (CoV2), the virus responsible for COVID-19 is known to specifically infect sustentacular cells but not olfactory sensory neurons (OSNs) in the olfactory epithelium (OE). Previous studies suggested that disruption of OSN nuclear architecture or persistent inflammation might be potential causes for CoV2-induced anosmia. However, the detailed underlying mechanisms and the infection patterns of different CoV2 variants have not been fully characterized. In this study, we analyzed the CoV2 infection pattern in the OE across different circulating variants and their impact on transcription in the olfactory mucosa of K18-hACE2 transgenic mice. By mapping viral variant infection patterns with detection of CoV2 nucleocapsid protein, we observed that omicron variant rarely infects olfactory mucosa while other tested strains are effective in their infection. Despite the sparseness of CoV2 infection in sustentacular cells, rapid and widespread antiviral responses were observed in the OSNs by in situ hybridization. Single cell RNA-seq analysis identified that around 57.4% of the OSNs are impacted, demonstrated by upregulation of antiviral genes. Within this OSN population, we observed suppression of mitochondrial DNA-encoded genes essential for ATP synthesis, and down-regulation of neuronal activity-dependent genes, which are

essential for neuronal function and plasticity. Our findings are significant in indicating that the molecular regulatory failures in OSNs may contribute to the mechanisms of CoV2-induced anosmia.

140 **Olfactory Receptor Co-Expression In The Mosquito Non-Canonical Olfactory System**

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Vector-borne diseases are estimated to kill over 700,000 people per year, 90% of which are due to diseases spread by mosquitoes. Understanding the mechanisms of odor sensation and host seeking in mosquitoes will allow us to develop more effective repellents and lessen the impact of these serious diseases. New findings have reported that the host-seeking mosquito *Aedes aegypti* exhibits a non-canonical olfactory system organization wherein olfactory sensory neurons can co-express more than one olfactory receptor, contrary to the traditional understanding of mammalian and insect olfactory system organization. Olfactory and ionotropic receptors are made up of co-receptor subunits necessary for receptor function and tuning receptors which define the responses of the receptor complexes. Previous data demonstrates co-expression of the olfactory co-receptors ORCO and Ir25a in the *Ae. aegypti* antenna and suggests that co-expression of tuning receptors of both olfactory receptors classes is not uncommon. Using Hybridization Chain Reaction fluorescent RNA *in situ* hybridization (HCR-FISH), I confirm co-expression of tuning receptors in the *Ae. aegypti* antenna. Furthermore, I investigate whether there is co-expression of Olfactory and Ionotropic tuning receptor subunits. Finally, I show preliminary data that relates expression of receptors in the antenna to responses in the *Ae. aegypti* antennal lobe. Understanding receptor co-expression as well as olfactory sensory neuron interconnectivity in the mosquito olfactory system will give us insights into the mechanisms these insects use when finding their human hosts and allow us to make informed decisions when investigating mosquito repellants and other methods to disrupt mosquito host-seeking.

142 **Vasopressin Elicits Functional Responses In Salt- And Putatively Sour-Sensitive Human Fungiform Taste Bud Cells**

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The sense of taste is mediated by the interaction of chemical stimuli with receptors expressed on taste bud cells (TBCs). Recent studies show that an array of hormones also interact with TBCs and may modulate TBC signaling. Arginine vasopressin (AVP) is best known for its role in regulating social behavior via CNS signaling. Peripheral AVP secretion, triggered by dehydration and osmotic challenge, is responsible for maintaining systemic water balance. AVP has been shown to impact ENaC expression and functional responses to salty and sour stimuli in mammalian and bullfrog TBCs. Yet, it is unknown if AVP directly impacts functional responses in human TBCs. We conducted qRT-PCR to determine if AVP receptors were expressed in cultured human fungiform TBCs. One type of AVP receptor, 1A (V1AR), was indeed expressed in human TBCs, along with V1BR, albeit to a lesser extent. Immunocytochemistry validated V1AR expression in human TBCs. Calcium imaging showed that AVP triggered robust calcium responses in a dose-dependent manner that were abolished in the presence of a V1AR antagonist. We found that 75% of TBCs responding to AVP also responded to KCl, which functionally identifies type III TBCs that are typically sour-responsive. Half of these cells also responded to salt (NaCl). We did not observe functional overlap with other taste modalities. Ongoing experiments are exploring the responsiveness of these cells to sour (acidic) stimuli and reproducing this work in acutely isolated murine TBCs. These data indicate that AVP could play a significant role in peripheral taste signaling, particularly with salt and sour responsiveness. Such modulation may occur in the context of organism-level changes in physiological state, such as dehydration, which may then trigger compensatory shifts in food and water intake.

144 **Investigating Taste Bud Cell Lifespan: In Vivo Imaging Of Taste Bud Cell Maturation And Turnover**

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The dynamic nature of taste buds, characterized by continuous cell turnover, was first identified through radioactive labeling studies. Post-mortem analyses estimate an average lifespan of 10 days for all taste bud cells, with Type II taste bud cells averaging 8 days and Type III taste bud cells 22 days. A critical barrier to understanding these dynamics *in vivo* has been an inability to observe and track individual taste bud cells in live mice. A more complete depiction of taste bud cell lifespan can be captured by tracking the same taste bud across time to determine how long individual cells spend in each stage of their life cycle (precursor, mature cell, etc.). Here, we measured the time individual cells spend as postmitotic precursor cells and the lifespan of mature Type II and III taste bud cells using *in vivo* two-photon microscopy. To assess postmitotic precursor cell development, *Shh*^{CreERT2} mice were crossed with *T1R3*^{GFP} or *GAD67*^{GFP} mice. Preliminary data show that Type II cells began differentiating as early as 3 days and Type III cells as early as 4 days post-tamoxifen injection. We evaluated the longevity of differentiated Type II taste bud cells in *T1R3*^{GFP} mice, and Type III taste bud cells in *GAD67*^{GFP} mice. Our observations reveal a range of cell lifespans, with both Type II and Type III cells having two subpopulations, one that is short-lived (some as short as 2 days) and another that is long-lived (some more than 22 days). These data indicate that differences in mean lifespan between Type II and Type III cells is due to differences in the ratios of short-lived to long-lived cells for each cell type. These findings emphasize the variability in taste bud cell longevity and highlight the necessity of longitudinal tracking to deepen our understanding of their life cycle and turnover rate.

146 **Interaction Of Fatty Acid Signaling In The Gustatory And Immune System**

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Dietary fatty acids play critical roles in both the gustatory and immune systems. In taste, they serve as the sapid molecules that underlie the ability to taste fat whereas in the immune system, they serve as messengers that help facilitate the fuel-based reprogramming of macrophages (MΦ) that underlie optimal immune function. It has become clear in recent years that there is a functional interaction between the taste and immune system and fatty acid signaling pathways serve as one focus of this overlap. As a first approach, in the present study, we are beginning to explore the interaction between taste and immune function by exploring the direct effects of fatty acids on MΦ polarization from M0 into M1 or M2 phenotypes using both RAW 264.7 cells and acutely isolated MΦs. Similar to taste receptor cells (TRCs), MΦ express G protein-coupled fatty acid receptors GPR120 and GPR84 and our calcium imaging assays reveal they respond over a similar concentration range. We are examining the effects of acute and long-term fatty acid stimulation of TRCs and MΦs on receptor expression and cellular responsiveness using biochemical, electrophysiological, and imaging assays. Our data show changes in MΦ phenotype in response to stimulation with saturated and unsaturated fatty acids and subsequent changes in cytokine release. TRCs are known to express a variety of cytokine receptors, including IFN-γ, TNF-α, and IL-1ß, and may serve as the target for these different M1- and M2-mediated cytokines and provide a pathway for immune modulation of taste. TRCs, as well, release cytokines that, in turn, may influence immune function. We will present data that reflects efforts toward our eventual goal of understanding this relationship between gustatory and immune system function.

148 **Unraveling Geniculate Ganglion And Trigeminal Ganglion Innervation Of The Lingual Epithelium**

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Both Geniculate Ganglia (GG) and Trigeminal Ganglia (TG) neurons convey mechanosensory information and innervate the same regions of taste papillae outside of taste buds (TBs). However, the organization of TG versus GG fibers remains unclear. Recent studies identified RET+ neurons in GG and TG that are responsive to stimulation of the tongue surface. The four glial cell line-derived neurotrophic factor (GDNF) family ligands (GFLs), GDNF, Neurturin (NRTN), Artemin (ARTN), and Persephin (PSPN), bind to their respective GFRα receptors (GFRα1-4) and subsequently activate RET. We found that GFRα1 and GFRα3, receptors for GDNF and ARTN, are expressed on fibers innervating intragemmal and extragemmal areas of fungiform taste buds. To distinguish between GG or TG originated RET+ fibers in the tongue, we compared the RET+ fibers from *Ret*-CreER reporter and *Ret*-CreER; *Phox2b*-Flpo dual reporter mice (that selectively label RET+ neurons from GG). Nearly all taste buds in *Ret*-CreER reporter mice had RET+ fibers innervating extragemmal regions, while only 60% of fungiform taste buds had extragemmal fibers labeled in the GG-specific reporter mice. Additionally, we found that Ret-expressing fibers innervate filiform papillae and that GG-fibers innervate many of these. Lastly, to delineate GG and TG contributions to GFRα1+ and GFRα3+ innervation, we performed unilateral transections of the chorda tympani (GG) and lingual (TG) nerves. Post-transection analysis showed that most GFRα3+ fibers within taste buds derive from the GG, whereas extragemmal GFRα1+ fibers mainly originate from the TG. In summary, TG and GG neurons exhibit distinct innervation patterns within the lingual epithelium.

150 **Maximizing Flavor: Leveraging Nano-Biophysical Methods For Studying Flavor Active Chemo- And Mechanosensors**

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The food industry faces the challenge of creating healthier products with less salt, sugar, fat, and calories while preserving flavor and consumer satisfaction. Flavor perception, shaped by taste, smell, texture, and individual factors, demands deeper understanding to advance healthier food innovations. This research employs nano-biophysical techniques, particularly bio atomic force microscopy (AFM), to explore taste and texture at the molecular level [1,2,3]. AFM provides nanoscale insights into food components' interactions with sensory receptors (taste and mechanoreceptors), and their role in flavor release. For example, AFM identified binding of a bitter peptide (VAPFPEVF) to its receptor (TAS2R16) without triggering downstream signaling. It also offers nanomechanical probing capabilities to study oral texture perception (mouthfeel), mediated primarily by mechanoreceptors in the oral cavity. Despite its significance, oral texture perception remains underexplored at the biomolecular level, particularly regarding links between food composition (e.g., food-derived agonists for mouthfeel), structure, and sensory responses [1, 3]. By integrating AFM with biochemical assays, molecular simulations, and human sensory evaluations, this research bridges objective measurements and subjective flavor experiences. It provides innovative approaches to decode chemo- and mechanosensory processes in flavor perception and offers novel concepts for designing healthier, sensory-appealing foods that address critical health and nutrition challenges. [1] Koehler, M, et al. Nat. Food (2024): 1-7. [2] Karanth, S, et al. J. Agric. Food Chem. 72.26 (2024): 14521-14529. [3] Karanth, S, et al. Foods 13.21 (2024): 3411

152 **Conditional Genetic Deletion Of Ace2 In Taste Buds Alters Peripheral Taste Function And Taste Bud Composition In Male Mice**

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Angiotensin-converting enzyme 2 (Ace2) is the primary receptor through which severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) enters host cells, leading to loss of taste, smell, and chemesthesis by unknown mechanisms. Ace2 stabilizes the renin-angiotensin-aldosterone system (RAAS), reducing inflammation, blood pressure and managing fluid balance in various tissues. Following viral entry, Ace2 is downregulated, causing RAAS dysregulation. We observed high levels of Ace2 mRNA expression in circumvallate papilla and anterior tongue of wild type mice. However, the biological role and expression of Ace2 in the taste system are not well understood. To explore this, we developed two mouse strains: Ace2fl/fl: K14-Cre,"Ace2 cKO," to conditionally delete Ace2 from taste buds and neighboring epithelial cells, and Ace2CE/+: Rosa26-tdTomato, a tamoxifen-inducible reporter strain. Ace2 expression in anterior taste buds of induced female reporter mice was increased compared to corn oil controls in preliminary studies. Recordings from the chorda tympani nerve of Ace2 cKO mice revealed specific changes in responses to sweet and sour stimuli in males but not females. Following these functional observations, we investigated the composition of taste bud cells, finding a significant increase in type II sweet-sensing cells and a decrease in type III sour-sensing cells. These results indicate that Ace2 regulates peripheral taste responsiveness in males by altering the balance of taste cells. The density of CD68+ macrophages or CD45+ pan immune cells was similar in cKO vs. control animals across sexes, indicating that conditional Ace2 deletion alone does not stimulate lingual inflammation. Studies in progress are measuring taste function and immune responses in Ace2 cKO animals under inflammatory conditions.

154 **Not So Sweet: Investigating The Role Of Receptor Tyrosine Kinases In Taste Homeostasis**

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Taste is mediated by taste buds housing 50-100 continuously renewing, short-lived taste receptor cells (TRCs) comprising type I cells (glial-like), type II cells (sweet-, bitter- or umami-sensitive), and type III cells (sour-sensitive). Since TRCs are continuously renewing, pharmacological agents that impede homeostatic pathways can dysregulate renewal and lead to taste dysfunction, or dysgeusia. Dysgeusia is a common symptom associated with oral chemotherapy drugs called tyrosine kinase inhibitors (TKIs), which inhibit receptor tyrosine kinases (RTKs). However, the role of RTKs has been entirely unexplored within the context of adult taste homeostasis. To evaluate if inhibition of RTKs could hinder taste homeostasis, we treated lingual organoids with three TKIs that commonly cause dysgeusia (axitinib, cabozantinib and sunitinib). Surprisingly, TKI treatment in organoids specifically decreased expression of Tas1r2, a marker of sweet-sensing TRCs. Treating mice with cabozantinib caused a decrease in the number of Tas1r2+ sweet cells while not affecting the overall number of type II cells. We also show through two behavioral assays that cabozantinib-treated mice have a blunted response to sweet tastants. Finally, we identified the RTK c-Kit as a candidate regulator of sweet cell homeostasis, as c-Kit is inhibited by all TKIs we tested and is expressed highly within sweet cells. Similar to the drug treatment, inducible knockout of c-Kit from type II cells significantly decreased the number of Tas1r2+ cells while not affecting the overall number of type II cells. These results suggest that c-Kit is necessary for the differentiation and/or maintenance of Tas1r2+ sweet cells, and that c-Kit inhibition by TKIs causes dysregulation of sweet cells that underlies TKI-induced dysgeusia.

156 **Sox9+ Epithelial Cells Are Multipotent Progenitors In Circumvallate Taste Papilla/Von Ebner&Rsquo;S Salivary Gland Complex Homeostasis**

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Taste is essential to distinguish between harmful and nutritious substances and is mediated by taste buds (TBs) on the tongue. Taste is facilitated by saliva that aids in breakdown of food and thereby, the release of tastants.

The murine circumvallate taste papilla (CVP) in the posterior tongue houses hundreds of TBs, each containing ~60 taste receptor cells that are constantly renewed from proliferating progenitors. The CVP epithelium connects ventrally with ducts of Von Ebner's minor salivary glands (VEG), which also undergo cell renewal; together they form one CVP/VEG complex (CVCx). Immunostaining and bioinformatic data suggest the transcription factor SOX9 marks epithelial cells at the junction of the CVP and VEG, while pseudotime analysis of CVCx scRNAseq data suggests that CVP and VEG epithelia arise from a common SOX9+ progenitor population. To test this, we used *in vivo* lineage tracing of SOX9+ epithelial cells and assessed the lineage potential of isolated SOX9+ cells using organoid technology. In $Sox9^{CreERT2}$;$Rosa26^{tdTomato}$ mice 2 days post-tamoxifen (pt), Tomato+ epithelial cells are located at the CVP/VEG junction, while 12 months pt, Tomato+ cells expand into CVP taste buds and non-taste epithelium, indicating SOX9+ cells are CVP progenitors. As SOX9 is constitutively expressed by most VEG cells, we could not determine if SOX9+ progenitors function in VEG renewal in vivo. However, isolated Tomato+ cells from $Sox9^{CreERT2}$;$Rosa26^{tdTomato}$ mice 24 hours pt generated organoids that house both salivary and taste lineages as assessed via marker expression and morphology. These data imply, at a population level, that SOX9+ CVCx epithelial cells are progenitors for both taste and salivary lineages. Support: T32GM141742, FDC021632A to TJI; DC018489, DC012383 to LAB.

158 **Degrading Synapses In The Taste Bud**

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The epithelial-derived taste cells of taste buds are renewed continuously throughout life. New, post-mitotic cells enter at the base of the bud, while older cells eventually die. To accommodate this renewal, taste nerve fibers must continuously remodel, separating from dying taste cells and forming synapses with new taste receptor cells. Here, using a high resolution, volumetric dataset attained by serial blockface scanning electron microscopy (sbfSEM), we examine the ultrastructural aspects of presumed degrading synapses between dying taste cells and nerve fibers. Many dying taste cells, as identified by ultrastructural features consistent with apoptosis, maintain recognizable synaptic structures at points of contact with afferent nerve fibers. In dying Type II cells, the atypical mitochondria that mark synapses are present, but their cristae appear more irregular or "loose" compared to the tightly packed tubular cristae of healthy Type II cells. In dying Type III cells, points of contact with nerves feature clusters of irregular vesicles larger (30-300 nm in diameter) than typical 40-60 nm synaptic vesicles. Whether these degenerating synapses are capable of synaptic transmission is unknowable with our current methods. Interestingly, many of the afferent nerve fibers appear to be nerve fiber fragments that no longer connect to the main intragemmal nerve fiber network. Such fragments suggest that nerve fragmentation may be a part of the nerve remodeling process.

160 **The Roles Of The Transcription Factor Spib In The Taste Papillae.**

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We recently showed that type II taste cells may mediate mucosal immune surveillance. They express Spib, a transcription factor that plays a key role in mucosal immunity in microfold (M) cells. *Spib* knockout ($Spib^{KO}$) mice have heightened attraction to sweet and umami tastants and a were dramatically altered taste cell. Recent scRNASeq experiments showed that duct cells of the circumvallate and foliate papillae -associated Von Ebners' gland might also be involved in mucosal immunity. scRNASeq and histological experiments showed that taste papillae contain a higher density of immune cells compared to neighbouring non-taste tissue. Expression of *Spib* and other M cell marker genes in taste and duct cells were upregulated upon administration of the M cell specific growth factor RANKL. To dissect the roles of SPIB in taste and duct cells, we developed a *Spib* conditional knockout ($Spib^{CKO}$) mouse strain. Tamoxifen-induced *Spib* ablation in this strain triggered severe inflammation in the taste papillae and lingual epithelium and downregulated the expression of multiple taste marker genes. Bulk RNASeq was used to determine the changes in gene expression in taste buds and Von Ebners' gland duct cells. Further analysis of changes in taste responses and mucosal immune responses will shed light on the roles of SPIB in taste signaling, taste cell regeneration and mucosal immunity.

162 **Postural Avoidance Reactions To Unpleasant Odors And Pictures**

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One of our sensory systems' key functions is to detect threats in the environment. Stimuli that we perceive as frightening or disgusting, i.e. negative, trigger instinctive avoidance reactions, and this core survival mechanism is believed to be expressed as subtle non-conscious postural reactions, even in experimental settings where participants are instructed to stand still. This early avoidance has so far mainly been studied using either indirect measures that make participants aware of their posture (e.g. force-plate based methods) or dependent on explicit cognitive tasks, such as asking participants to move a joystick to indicate an urge to approach or avoid the stimulus. Therefore, the underlying mechanisms of this basic survival strategy are still poorly understood. Here, we used a 3D-camera based method which allows direct measures of postural reactions with millimeter precision while participants are kept naïve to the purpose of the experiment. We tested this novel technique in two different modalities: olfaction and vision. In the olfactory experiment, we presented participants with 6 different odors and

asked them to verbally rate their perceived valence on each trial to identify individual preferences. We found that following presentation of subjectively unpleasant odors, participants moved away from the stimulus source, as compared to pleasant odors. We found the same pattern of results in the (pre-registered) visual experiment. Our results demonstrate a putative modality-nonspecific early proxy for avoidance behavior as a response to perceived negative valence. In addition, the results demonstrate the validity and general applicability of this novel measure and present a new promising experimental paradigm for assessments of non-conscious approach-avoidance responses in humans.

164 **Odor-Taste Mixture Experience Modulates Odor Concentration Preference In Rats**

Dinna N. Ferreira, Caitlin J. White, Chad L. Samuelsen
University of Louisville, Louisville, KY, United States

Taste concentration is a key determinant of palatability; for example, higher sucrose concentrations are preferred over lower ones, while the reverse is true for citric acid. However, food preference is not solely determined by taste. Flavor perception arises from the interaction between taste and smell, where sampling an odor-taste mixture drives strong associations between the odor and the taste's identity and value. Yet, the role of odor concentration, independent of taste, in guiding consummatory preferences remains unclear. To investigate this, we used a 2-bottle brief-access task to test two groups of female rats for preferences between two concentrations of isoamyl acetate (low 0.01% and high 0.1%). Each group then experienced both odor concentrations paired with a fixed concentration of either sucrose (100 mM) or citric acid (30 mM). Across all conditions, both groups preferred the low odor concentration. However, compared to pre-mixture experience, pairing with sucrose increased consumption of the high odor concentration, while pairing with citric acid further reduced its consumption. These findings demonstrate how odor concentration influences consummatory choice. While lower concentrations are generally preferred, odor-taste mixture experience with sucrose increases the preference for the high odor concentration, while mixture experience with citric acid lowers it. This is consistent with other multisensory research demonstrating that more salient stimuli, in this case the higher odor concentration, more strongly influences consummatory behaviors dependent upon odor-taste associations.

166 **Modulations Of Corticospinal Excitability And Effective Connectivity In Response To Odorants With Different Hedonic Value In Depression**

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Olfactory stimulations trigger motor behaviors, such as approaching pleasant odorants and avoiding unpleasant ones. Recent studies, using electroencephalography and transcranial magnetic stimulation (TMS) have revealed a link between the olfactory and motor (M1) systems. Neuroimaging studies have shown that odorants influence dorsolateral prefrontal cortex (DLPFC) connectivity, which in turn modulates M1 activity. Changes in DLPFC-M1 connectivity occur during approach/avoidance behaviors in healthy controls (HC). However, this relationship has not been yet explored in psychiatric disorders with altered hedonic processing, such as major depressive disorder (MDD), which is associates with olfactory dysfunction, maladaptive approach-avoidance behaviors, and impaired DLPFC activity. These alterations may also be mediated by childhood trauma. In this study, we investigated how pleasant and unpleasant odors modulate corticospinal excitability and DLPFC-M1 connectivity in MDD, aiming to identify neurophysiological markers and improve our understanding of olfactory-motor interactions. We developed a method using a breath-synchronized olfactometer to coordinate TMS and odorant stimulations. Preliminary results showed no significant interaction between odorant hedonic value and group. However, in HC, pleasant and unpleasant odorants tended to increase excitability and connectivity, while patients tended to show reductions, except for a slight facilitation with pleasant odorants. A significant negative correlation was found between DLPFC-M1 connectivity following unpleasant odorant and childhood trauma. This provides a new approach to assess hedonic odor perception and its impact on brain connectivity and excitability, paving the way for future studies on odor-based biomarkers in neuropsychiatric disorders.

168 **Sleep Phenotype Of Evening Chronotype And Sweet Taste Preference Drive Added Sugar Intake**

Sierra Aguilar, London Caceres, Changqi Liu, Jing Zhao, Surabhi Bhutani
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Evening sleep chronotype (EC), characterized by preference for late bedtime and activity, has been linked to increased intake of added sugar, contributing to obesity. However, the mechanisms underlying this dietary behavior remain unclear. Here we examine if increased sugar intake in EC is explained by heightened preference for sweet taste. Sixty-two participants (26.2 ± 9.3 years) were classified into morning (MC, n=15), intermediate (IC, n=32), or EC (n=15) chronotypes using the Morningness-Eveningness Questionnaire. Fasting participants completed a sweet taste preference task and an in-lab food choice and intake task. Habitual diet intake was recorded using a 3-day food diary. EC reported a higher sweet taste preference (470 ± 208 mM sucrose) compared to MC (402 ± 212 mM) and IC (387 ± 183 mM), although differences were not significant. Sweet taste preference was positively associated with added sugar intake in habitual diet ($r=0.29$, $p = 0.03$) and total caloric intake from in-lab sweet and savory snacks ($r=0.30$, $p = 0.02$). Regression analysis showed that EC individuals consumed an additional 4.56 tsp of added sugar per 1,000 kcal compared to MC ($p = 0.04$), and sweet taste preference independently predicted added sugar intake ($\beta = 0.02$, $p < 0.001$). However, an interaction indicated

that increased sweet taste preference among EC participants was associated with reduced added sugar intake ($p = 0.01$). This unexpected finding suggests that EC individuals with high sweet taste preference may regulate their sugar intake more effectively than other dietary components, potentially due to health concerns, despite reporting lower cognitive restraint ($p = 0.03$). These findings highlight a complex interplay between chronotype, taste preference, and added sugar intake that warrants further investigation.

170 **Repeated Sodium Depletion Increases Sodium Consumption And Decreases Reward Sensitivity As Assayed By Intracranial Self-Stimulation**

Rachel M Donka, Jamie D Roitman
University of Illinois Chicago, Chicago, IL, United States

Physiological need states invigorate goal-directed behaviors to restore homeostatic balance, engaging sensory and motivational pathways. Neural circuits that command motivated behaviors are engaged by the positively reinforcing properties of obtaining the needed stimuli or by the alleviation of need-induced negative affect. Previous work from our lab demonstrated that chronic, but not acute, fluid restriction reduced sensitivity to brain stimulation reward. The maintenance of fluid and sodium balance are linked, with sodium need eliciting strong goal-directed behavior. Multiple depletions drive escalating behavior to seek and consume sodium, modulating the palatability of high concentrations of sodium. Unknown are the mechanisms by which changes in need states modulate reward sensitivity, as well as how sensitivity shifts in response to repeated homeostatic challenges. To address this question, we used intracranial self-stimulation (ICSS) in rats with acute sodium depletion induction (furosemide, 10 mg/kg, sc) once per week for four consecutive weeks. Stimulating electrodes were implanted in the medial forebrain bundle and animals were trained to lever press for stimulation ($n = 16$). Using a rate-frequency protocol we determined the threshold stimulation frequency (theta) that was reinforcing for each subject and measured how sodium depletion altered theta in a within-subjects design. We found increased ICSS theta values, indicating a decrease in reward sensitivity over four sodium depletions. Sodium intake in the 1-hour post ICSS intake period increased across the four depletion sessions. Sodium intake post sodium depletion also increased across weeks. Collectively, these results suggest that repeated sodium depletion decreases reward sensitivity, while driving increased consumption of sodium.

172 **The Ingestive Response Reflects Neural Dynamics In The Gustatory Cortex**

Natasha Baas-Thomas, Abuzar Mahmood, Kathleen Maigler, Yixi Wang, Donald B. Katz
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When a taste stimulus reaches the tongue, the gustatory system has one basic goal - to determine whether that stimulus should be consumed or expelled from the mouth. Rats exhibit stereotyped and distinct orofacial movements that reflect the hedonic value of a tastant. The primary aversive-related orofacial movement, gapes, is easily detected experimentally which has led several studies to investigate the neural signals driving the rejection of a tastant. In this study, we aim to better understand the signals guiding and reflecting the decision to ingest a palatable tastant. We developped a machine learning classifier capable of discriminating individual aversive and ingestive-related orofacial movements from electromyographic (EMG) activity of the jaw opener (anterior digastric) muscle. Our findings indicate that mouth movements associated with ingestion can be further divided into distinct subtypes. We analyzed the timing of these behavioral subtypes relative to neural activity in the primary gustatory cortex (GC), where taste responses transition through three firing-rate “epochs”. The transition to the late epoch has previously been shown to modulate the onset of gaping, and preliminary results indicate a similar correlation between GC dynamics and the ingestive-related mouth movements. These insights deepen our understanding of how sensory information in the GC is transformed into context-appropriate motor outputs.

174 **Genes To Glass: Role Of Genetic Heritability In Alcohol Preferences And Sweetener Effectiveness**

Ha Nguyen[1], Cailu Lin[1], Katherine Bell[1], Amy Huang[1], Alissa Nolden[2], Paule Joseph[3], Danielle Reed[1]
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Sweeteners, including sucrose, are often used to reduce bitterness in alcoholic beverages, contributing to higher consumption of alcohol and sugars. However, not everyone perceives bitterness similarly, partly due to genetic variation. To better understand genetic influences on alcohol perception, intake and sweetener effectiveness, we tested genetically informative adults (twins/triplets N=219; singletons N=7) for their sensory perception (bitterness, sweetness, saltiness, burning) and liking of five ethanol concentrations (0%, 8%, 32%, 16% presented with and without 0.67M sucrose), questionnaires (AUDIT—Alcohol Use Disorders Identification Test, food liking) and saliva sample for genetic analysis. Most participants (91%) were low-risk drinkers, and AUDIT score correlated with liking of favorite alcoholic drink (R=0.38), vodka (0.38), scotch or whiskey (0.31), bitter beer (0.31), and spirit soda (0.29). Adding sucrose significantly decreased bitterness, increased sweetness, and shifted preference from dislike to like, though individual differences were large. Heritability analyses (structural equation modeling, SNP-based) showed significant heritability for the liking of 8% ethanol (h^2=0.36;0.26), 16% ethanol + sucrose (0.31;0.39), and sucrose alone (0.19;0.27). Although no apparent heritability emerged for sucrose’s ability to reduce bitterness, SNP-based analysis suggested genetic influence (0.31) on sucrose effectiveness in ethanol liking. AUDIT score and reported liking of alcoholic beverages (spirits with soda, wine, margaritas/daiquiris, vodka, scotch or whiskey) were also heritable. These findings highlight that genetics partially influences the liking and intake of alcoholic drinks with and without sucrose, with potential implications for personalized dietary and intervention strategies.

176 **Hedonic Bias In Perception Of Opposing Olfactory Stimuli**

Abby B. Finkelstein[1], Ariana Glick[2, 1], Elizabeth Daramola[3, 1], Venkatesh N. Murthy[1]

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The world constantly presents animals with conflicting sensory information, to which they respond with approach or avoidance based on their current internal state. Our project focuses on how opposing cues are resolved to make sensory decisions. In the presented task, head-restrained mice learn to lick or avoid licking in response to binary mixtures of punished and rewarded odors in which the dominant component predicts outcome. Trained mice are presented with eight randomized binary mixtures including trials of 50/50 ratios. Mice's likelihood of licking depends on the proportion of rewarded odor and generalizes to novel ratios, indicating that performance is based on perceived odor dominance rather than mixture recognition. Ambiguous mixtures lead to variable but positively skewed decision making. To study how such decisions can be flipped by acute states, we induced an anxiety-like state using non-invasive, naturalistic exposure to bright light prior to task initiation. The anxiety-like state shifts decision making in our task in males but not females, driving less risk-averse and faster decision making on ambiguous trials while preserving performance on easy ratios. Our task thus enables us to ask how the olfactory system quickly alters its weighing of olfactory information. The neural dynamics giving rise to opposite responses trial-to-trial and to the global shifting of responses across states are likely reflected in the olfactory tubercle (OT) of the ventral striatum. Ongoing experiments employ cellular resolution multiphoton calcium imaging of the OT throughout the task, in tandem with pupillometry and facial recordings to interrogate emotional and attentional dynamics. These experiments aim to uncover the mechanisms of cognitive bias in sensory decision making.

178 **Neophobia Attenuation And Neuronal Response Fidelity Within The Gustatory Cortex**

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Food neophobia is an evolutionary trait in animals, where mice limit consumption of novel tastes until their hedonic value and aftereffects are determined. The Gustatory Cortex (GC), located in the insular cortex, is thought to be the primary regulator of neophobia, although the exact mechanism remains unclear. Recent studies have explored changes in neuronal responses through c-Fos expression or alterations in coding patterns via electrophysiological recordings in head-fixed mice. In this study, we use microendoscope calcium imaging to examine changes in both coding and the number of neurons involved. Over 600 individual neurons were tracked in eight animals over four consecutive days. Freely moving mice were presented with randomized trials of water or saccharin. Saccharin consumption was lower on Day 1 and increased over subsequent days, indicating a reduction in neophobia (AN). Statistical analysis of the mean taste-evoked change in response (ΔF) revealed no significant change in the number of saccharin-responsive GC cells or their response strength. However, further analysis revealed differences in GC coding on the neophobia day, with less consistent trial-to-trial responses for saccharin compared to subsequent days. Further, during neophobia, we found no relationship between representational similarity and licking behavior for each stimulus. However, as neophobia attenuated, this relationship stabilized, whereby representations of water and saccharin diverged as saccharin preferences emerged. These findings suggest that AN is not reflected in population changes in neuronal excitability but rather a product of multiple subtle changes in neuronal signaling, leading to greater response fidelity among neurons in the gustatory cortex as novel tastes become familiar.

180 **Anxiety-To-Eat Is Dependent Upon Sensory Modality And Caloric Density Of Foods In Anorexia Nervosa.**

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

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Ingestive behaviors are controlled by homeostatic and non-homeostatic regulatory signals. However, in anorexia nervosa (AN), these signals are overridden to achieve or maintain low body weight. The mechanisms by which AN disrupts normal regulatory circuits remain unclear. Increasing evidence indicates dietary restraint in AN is driven by anxiety associated with consuming calorically dense foods. We investigated the impact of internal (fullness) and external (olfactory and visual food cue) signals in eliciting anxiety-to-eat in women with AN (N=20) and healthy control women (HC; N=34) following an overnight fast. In response to suprathreshold olfactory cues (Sniffin' Sticks) and visual cues (images) of higher (HED) and lower energy-dense (LED) foods, participants rated their level of anxiety-to-eat (visual analogue scale; 0=no anxiety, +100=most anxiety ever experienced). Participants also provided ratings for liking and perceived fullness to consume one standard portion of each food. Regardless of cue category, anxiety-to-eat was greater in AN than HC. Response profiles were similar between groups for visual but not olfactory food cues; the AN group showed greater anxiety to eat HED relative to LED foods in response to visual and olfactory cues, whereas the HC group showed greater anxiety to eat HED relative to LED foods in response to visual cues only. Anxiety-to-eat elicited by visual HED food cues was positively correlated with perceived fullness in AN and negatively correlated with food liking in HC. These preliminary findings indicate that food liking and external food cues influence anxiety-to-eat in HC. However, anxiety-to-eat is dependent upon sensory modality and calorie density, and perceived internal state (fullness) may interact with external food cues to influence anxiety-to-eat in AN.

182 **Deet Inhibits Skin Penetration In A Skin-Invading, Human-Parasitic Nematode**

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Strongyloides stercoralis is a skin-penetrating, human-parasitic nematode that infects over 600 million people globally and can be fatal for immunocompromised individuals. While current medications help clear existing infections, they do not prevent infection and reinfection rates remain high in endemic areas. Although topical repellents are widely used to reduce the spread of insect-borne diseases, the possibility of using topical repellents to prevent nematode infections has not been investigated. We tested whether N, N-diethyl-meta-toluamide (DEET), a widely used insect repellent, affects the ability of *S. stercoralis* infective larvae to invade hosts by skin penetration. We performed *ex vivo* skin penetration assays using excised, epilated rat skin. Individual infective larvae were placed on rat skin evenly coated with either 30% or 50% DEET. Skin-penetration behaviors were then video-recorded and analyzed *post hoc*. We found that applying either 30% or 50% DEET to the skin surface greatly reduced skin penetration – whereas ~85% of the infective larvae penetrated into control skin, only ~30% of the larvae penetrated into DEET-coated skin. Moreover, the average time until the completion of penetration was delayed ~2-fold. Infective larvae exposed to DEET also exhibited novel behaviors on the skin surface, such as idling, reversals, and looping. We then extended our behavioral analysis to human skin samples and found that DEET similarly reduced penetration on human skin. We are currently investigating the molecular mechanisms by which DEET blocks skin penetration. Our results identify DEET as a strong candidate for parasitic nematode control and prevention.

184 **Effects Of A Cnv Relaxing Fragrance On Sleep**

Alba/T Cilia, Raphael/K/L Kang
Takasago International Corp. USA, Rockleigh, NJ, United States

Contingent Negative Variation (CNV) is an Evoked Response Potential (ERP) measured by electroencephalograph (EEG) that has been widely used to study the effect of odors on the brain. The principal axes of CNV are stimulating, relaxing, and no effect. Sleep is a critical process for the maintenance of good health as it affects both mental and physical health. As the number of hours and quality of sleep have been declining steadily in our modern society, there is an interest in finding ways to improve sleep and so health overall. We postulate that if we get the brain in a state of stimulation or relaxation, we may influence sleep. In our study, we examined the effect on sleep of a fragrance specifically designed with CNV relaxing odors. The study included fifteen participants exposed to a fragrance versus a no-door control for seven nights while sleeping. They wore a Fitbit® to monitor their sleep every night and filled out sleep diaries daily to self-report moods. Statistical analysis (ANOVA) of the Fitbit® sleep data showed a significant improvement in sleep when exposed to the CNV relaxing fragrance compared to the no-odor treatment. Results showed time spent asleep increased 49.8%, time awake decreased 53%, and deep sleep, a crucial stage of the sleep cycle known to support physical and mental recovery, increased by 20%. Self-report positive moods on awakening reported more often by the participants were "refreshed" "calm," and "energetic." The results of this pilot study support a connection between CNV-relaxing odors and sleep benefits. It shows fragrances designed with CNV relaxing odors may offer a non-invasive and natural means to improve sleep quality.

186 **Cyclic Nucleotide Signaling Regulates Carbon Dioxide Valence In *Caenorhabditis Elegans***

Ricardo F. Frausto[1,2], Ava E. Bignell[1], Elissa A. Hallem[1]
[1]Department of Microbiology, Immunology, and Molecular Genetics, University of California, Los Angeles, Los Angeles, CA, United States, [2]Molecular, Cellular, and Integrative Physiology PhD Program, University of California, Los Angeles, Los Angeles, CA, United States

Many chemosensory cues can be either appetitive or aversive depending on an animal's physiological and environmental context, yet how chemosensory circuits generate flexible behaviors is poorly understood. To identify the mechanisms that regulate chemosensory valence, we used the carbon dioxide (CO_2)-evoked behavior of the free-living nematode *Caenorhabditis elegans* as a model. The response of *C. elegans* to CO_2 is experience-dependent such that well-fed animals raised at ambient/low CO_2 are repelled by CO_2, while well-fed animals raised at high CO_2 and starved animals raised at low CO_2 are attracted to CO_2. We found that the cGMP-dependent protein kinase EGL-4 plays a key role in regulating CO_2 valence: well-fed *egl-4* loss-of-function (*lof*) animals raised at high CO_2 were repelled by instead of attracted to CO_2. Surprisingly, *egl-4* was not necessary for CO_2 attraction in starved animals, indicating that distinct mechanisms regulate CO_2 attraction in the context of prior CO_2 exposure vs. starvation. Expression of EGL-4 in the BAG neurons, a pair of CO_2-detecting neurons in the head, was sufficient to rescue the *egl-4(lof)* phenotype, demonstrating that EGL-4 acts in BAG to regulate attraction to CO_2. In addition, we found that CO_2 valence is also regulated by cAMP signaling. Animals lacking a functional *kin-2*, which encodes the regulatory subunit of the cAMP-dependent protein kinase PKA, have constitutively active PKA activity. We found that *kin-2(lof)* animals raised at low CO_2 are attracted to instead of repelled by CO_2. Thus, increased cAMP signaling may promote CO_2 attraction during starvation. Together, our results suggest a model whereby CO_2 valence is determined by the balance of cAMP and cGMP signaling, and this balance varies depending on the physiological and environmental context.

10:00 - 12:00 PM	Calusa EFGH
Non-Gustatory Orosensory Mechanisms That Dictate Whether to Eat or Not to Eat	

Chair(s): Snigdha Mukerjee & Stephen Roper

10:00 **Introduction**
Stephen Roper
University of Miami

Trigeminal Mechanosensory Mechanisms And Impacts On Food Choice
Yalda Moayedi
Pain Research Center, Department of Molecular Pathobiology, New York University College of Dentistry, New York, NY, United States

We use the sense of touch to guide essential oral functions, including flavor assessment, feeding, and speaking. The mechanisms underlying oral mechanosensation remain understudied compared to other oral sensations. Our prior work characterized the anatomical and physiological properties of oral mechanosensory neurons. We found that tongue-innervating mechanosensory neurons are both anatomically distinct and possess force-response relationships that are unique compared to canonical mechanosensory neurons. We aimed to understand the roles for mechanosensory ion channels in sensation. We tested whether lingual mechanosensory neurons utilize the principal mechanosensory ion channel, Piezo2, for mechanotransduction. We found that loss of Piezo2 in a subpopulation of tongue-innervating neurons reduced the fraction of stroke-sensitive neurons while introducing neurons with sustained responses to pressure. This suggests that Piezo2 is necessary for stroke sensitivity, but other mechanosensory ion channels are utilized to transduce pressure in tongue-innervating neurons. We find that this subpopulation of mechanosensory neurons expresses an array of alternative mechanosensory ion channels include Piezo1, TMEM63A, TMEM63B, and TRPV4, providing alternative mechanisms for pressure sensitivity. We next tested the roles of oral trigeminal neurons in transduction of flavors including oil and tannins. We find that different subpopulations of mechanosensory cells are mediate transduction of these varying flavor qualities. Our current work seeks to determine the roles of Piezo2 and subpopulations of lingual mechanosensory neurons in texture detection and transduction of astringency sensation.

Polak Young Investigator Awardee: Trigeminal Circuits Dictate Innate Rejection Thresholds For Ethanol Through Oral Chemesthesis
Snigdha Mukerjee, Yizhen Quan, Keaton Song, Aditya H. Bhatt, David B. Cohen, Vikrant R. Mahajan, Rachelle Larivee, Steven Pierce, Alex R. Brown, Zahra Z. Farahbakhsh, Kirsty Erickson, Cody Siciliano
Vanderbilt University, Nashville, TN, United States

Ethanol is highly unusual among acutely toxic chemicals in that it is readily consumed by essentially all animal species upon access. The central pharmacological effects of ethanol mediate its powerful reinforcing properties, but the neural mechanisms that control palatability of ethanol and explain innate preferences prior to intoxication are unknown. Further, chronic heavy ethanol drinkers often substitute noxious ethanol-containing products, suggesting that dysregulated drinking may be related to disruption of innate chemical defense systems responsible for oral rejection of toxins. Ethanol's complex flavor profile includes pronounced irritant/burning sensations, termed oral chemesthesis, which become dominant at high concentrations. Following oral stimulation with palatable (15%) v. chemesthetic (50%) concentrations of ethanol, whole-brain cfos mapping revealed chemesthetic-selective activation of multiple subnuclei in the spinal trigeminal nucleus. Single-cell sequencing of trigeminal ganglion and viral tracing from the tongue combined with whole-head clearing revealed TRPV1+ orotrigeminal ganglionic fibers anatomically positioned to transmit chemical concentrations from mouth to brainstem. Pharmacogenetic lesions of TRPV1+ trigeminal nerve cells produced a robust blunting of oral reactivity to ethanol, resulting in preference for low doses and augmented rejection thresholds for high concentrations. Endoscopic multiphoton through-brain imaging of single cell calcium dynamics in trigeminal ganglion during consumption of tastants and chemesthetics revealed ethanol-selective, concentration-dependent sensory coding. Together, we anatomically and functionally describe a peripheral-central circuit involved in mammalian chemosensation which controls palatability of ethanol.

Oral Trigeminal Perception Of Astringency, Capsaicin, And Stereognosis: Exploring Individual Variability And Impact Of Taste Dysfunction
Mariano Mastinu
Smell & Taste clinic, Department of Otorhinolaryngology, Technische Universität Dresden, Dresden, Germany

The perception of food is a multisensory experience that involves the interaction of taste, smell, and trigeminal sensations. Beyond taste receptors, the oral cavity contains receptors that respond to tactile, thermal, and painful stimuli. While taste sensitivity and its influence on food perception, preference and selection have been extensively studied, less is known on the variability in oral somatosensory perceptions and their role in taste dysfunction. Astringency, for example, is the “dryness” sensation of the mouth after consumption of tannins from red wine or berries. The identification of this stimulus varies according to familiarity and salivary proteins, and it is less recognized in patients with taste dysfunctions. On the other side, spiciness is another somatosensory perception linked to the trigeminal nerve. Additionally, oral stereognosis (the ability to recognize and discriminate forms) is detected thanks to mechanoreceptors, and conveyed through the trigeminal nerve. We designed a rapid test for gustatory and somatosensory stimulus identification to be implemented in clinical practice. Based on previous research it was hypothesized that a decrease in taste function affects trigeminal perceptions. With consequent observatory studies, we found that patients with taste dysfunction are less able to

identify trigeminal stimuli compared to a healthy population. Using a set of shapes with increasing size, we also observed that oral 3D shape recognition was less precise in dysgeusic patients than in healthy controls. Ageing had a negative influence on stereognostic ability, while gender had no effect. These results shed light on interconnection of gustatory and trigeminal systems in the oral cavity, which should be considerate for its impact on food perception.

Playing With Fire: If It Hurts, Why Do We Keep Eating It?

John E. Hayes[1,2]

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Ingestive behavior research in humans usually answers one of two questions: 'what do we eat?' or 'how much do we eat?'. Over the last 15 years, work from our laboratory has typically focused on the former, finding a nuanced relationship between food liking and intake. Regarding oral burn from capsaicin, we consistently find a cluster of personality traits – sensation seeking, variety seeking, risk taking, and sensitivity to reward – robustly predict liking and intake of foods containing chili peppers, a finding that has been replicated subsequently in larger cohort studies like the ItalianTaste project. More recently, we have used a series of standardized test meals to study how manipulation of oral heat potentially affects eating microstructure (e.g., eating rate), with downstream effects on energy intake. Specifically, we find increasing oral burn can substantially slow eating rate, and thus energy intake; critically, such manipulations do not depend on changes in liking. That is, we are not merely making the food unpalatable by making it too spicy to eat. This suggests capsaicin-driven changes in eating microstructure may be a viable strategy to slow eating rate and reduce ad libitum intake without adversely impacting the pleasure from food.

Neurobiology And Psychophysics Of Oral Chemesthesis

Earl Carstens
University of California, Davis

Although many foods and drinks contain chemicals that impart oral pungency by activating trigeminal pain pathways, they are nevertheless often preferred. Capsaicin and other agents elicit oral irritation by exciting chemonociceptors projecting to the brain via the trigeminothalamic tract. Lingual application of chemesthetic agents elicited c-fos expression in trigeminal subnucleus caudalis (Vc) and other areas. Single-unit recordings revealed that many individual Vc neurons responded to multiple irritant chemicals. The same applies for many individual trigeminal ganglion neurons based on calcium imaging. Thus, many first- and second-order trigeminal neurons are activated by a spectrum of irritants consistent with the idea of a "common chemical sense" (although chemospecific neurons may also exist). Rodents exhibit aversion to capsaicin in a dose-dependent manner. In human psychophysical studies, lingual application of many chemestheric agents elicited irritation, the intensity of which increased (sensitization) with repeated applications of capsaicin, piperine, citric acid or NaCl. In contrast, repeated application of nicotine, menthol, cinnamic aldehyde, allyl isothiocyanate or ethanol elicited irritation that decreased across trials (desensitization). Similarly, capsaicin or nicotine elicited contrasting patterns of firing in Vc neurons. Moreover, capsaicin and other chemesthetic agents cross-desensitized irritation, except for NaCl which cross-sensitized capsaicin-evoked irritancy. Why some people develop a learned preference for spicy food and carbonation is not well understood, but might involve physiological mechanisms such as euphoria due to pain-related release of endorphins, or personality traits such as risk-taking, impulsivity, or sensitivity to reward or punishment.

10:00 - 12:00 PM	Calusa ABC
Odor Quality Prediction	

Chair(s): Jessica Brann & Casey Trimmer

Odor Quality Prediction: Cracking The Odor Code
Jessica H. Brann, Casey Trimmer
dsm-firmenich, New York, NY, United States

In the last two decades, extensive research efforts have focused on a fundamental problem: can we predict the odor quality of monomolecular odorants, and if so, can we extend this ability to predict the odor quality of a complex odor blend? To predict odor quality, some approaches unify perceptual observations with odorant physicochemical parameters, while others also incorporate ligand-receptor relationships. In this symposium, we discuss approaches to date, and address the question of how data describing stimulus integration in peripheral olfactory receptors and the olfactory bulb can be used to predict monomolecular odorant quality, and how that answer may change when considering quality prediction for natural odors and/or odorant mixtures.

10:05 **Elemental Encoding At The Olfactory Periphery**
Daniel A. Raps, Lily Wu, Giulia Papiani, Georgia M. Pierce, Imraan Adat, Randy Arroyave, Jessica H. Brann, Patrick Pfister
DSM-Firmenich AG, 250 Plainsboro Road, Plainsboro, NJ 08536, USA

Odor percepts arise from the combinatorial interactions between volatile compounds and odorant receptors singularly expressed in olfactory sensory neurons. The resulting neuronal activity encodes the multiple olfactory qualities individual compounds or mixtures elicit. Taking advantage of perfumery ingredient descriptor datasets, we measured the descriptor distribution of human odorant receptor agonists as a function of receptor activity level. We quantified how individual human odorant receptors may uniquely encode singular olfactory qualities, akin to parallel encoding lines present in other sensory systems. In addition, we identified compounds that activate multiple receptors simultaneously, which in turn elicit the unique percepts associated with each receptor. This provides evidence that a peripheral elemental coding strategy encodes olfactory qualities.

Do Neurons Matter? Using Neural Recordings Of Odor Representations To Inform Predictive Models Of Odor Quality
Matt Wachowiak
Dept. of Neurobiology, University of Utah School of Medicine, Salt Lake City, UT, United States

Efforts to understand the relationship between odorant chemical structure and odor quality have made great progress in recent years, thanks in no small part to the power of machine learning approaches that couple chemoinformatics with olfactory psychophysics in humans. However, such approaches bypass a mechanistic understanding of odor perception and raise the question of whether understanding the neural mechanisms underlying olfactory sensation has anything to offer the odor quality prediction problem. I will review recent work from our laboratory in which we have characterized the odorant response specificities of a large fraction of the olfactory sensory neuron population in mice and explored the structural determinants of odorant receptor tuning in vivo. This work suggests that olfactory receptor specificities can be well-explained by straightforward chemical substructural features, but also that the determinants of tuning are heterogeneous across chemical space and across receptor subclasses. We have also found that perireceptor processes - in particular, the rapid metabolism of odorants in the olfactory mucosa - strongly shape the neuronal representation of odors in vivo and distort the apparent relationship between chemical structure and receptor specificity. I will discuss how these findings, arising from neuronal recordings in non-human animals, may lead to refined predictions and inform mechanistically-grounded models of odorant structure-quality relationships.

Predicting Human Olfactory Perception From Stimulus Chemistry
Emily J Mayhew
Michigan State University, East Lansing, MI, United States

A collection of hundreds of distinct molecules at concentrations spanning several orders of magnitude travel up our nasal cavities and activate some combination of several hundred olfactory receptors, which transmit signals to the brain, and in under a second, we've recognized the smell of coffee. How does the olfactory system translate such a chemically complex stimulus into odor perception, and can we learn to predict percept from stimulus chemistry? While receptor activation and cortical processing are essential for human olfactory coding, there are significant efficiencies in pursuing direct prediction of percept from chemistry. By leveraging odor-specific chemical features, odor characteristics for a single odorant can be predicted via a GNN model with reasonable accuracy (median R=0.49), representing an advance over previous models that used out-of-the-box chemical features. As the field sets its sights on odor mixture stimulus-to-perception modeling, there will be trade-offs in efficiency and diagnostic insights between consolidating or replicating individual steps in olfactory processing. This talk will discuss the state-of-the-art in chemistry-to-perception modeling and make the case for perception-to-perception modeling as an insight-rich strategy to advance odor mixture predictive models.

From Woody To Fruity: Leveraging Substructural Features For Odor Prediction Of Complex Mixtures
Doris Schicker[1], Satnam Singh[1,2], Jessica Freiherr[1,2], Andreas Grasskamp[1]
[1]Department of Sensory Analytics and Technologies, Fraunhofer Institute for Process Engineering and

Packaging IVV, Freising, Germany, [2]Department of Psychiatry and Psychotherapy, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany

The odor of a molecule is foremost characterized by its molecular structure. We previously showed that using a well-defined set of substructural features is an effective strategy to predict the odor of single molecules. In nature, however, perceived odors are often the result of a complex mixture of odor-active molecules. Evaluating or predicting the scent quality of these mixtures poses a significant challenge, not just for statistical models but also for trained assessors. We recently demonstrated that machine learning algorithms are able to predict key odor attributes of whiskies (American or Scotch) based on their molecular composition and substructural features. This was achieved by integrating data from analyses of 16 whiskies with sensory data from 11 panelists and applying machine learning algorithms. We used the linear classifier OWSum and a Convolutional Neural Network (CNN) to classify samples and predict sensory scores with high accuracy, surpassing panel assessments and enabling fast data-driven sensory evaluation in mixtures. This approach has high potential in many applications to support sensory assessments and provide a predictive framework for quick sample classification.

Integrating Chemical, Sensory, And Expert Knowledge Data For Predicting Odor Profiles In Complex Mixtures

Thierry Thomas-Danguin
Centre des Sciences du Goût et de l'Alimentation, INRAE, CNRS, Institut Agro, Université Bourgogne Europe, Dijon, France

Odor quality arises from the initial detection of volatile chemical compounds by olfactory receptors. Consequently, knowing the chemical composition of an odor stimulus should theoretically lead to an understanding of its odor quality. However, numerous studies indicate that this relationship is rarely straightforward. The list of odorants in an odor stimulus is often insufficient to predict the perceived odor of their mixture. This is because odor perception relies on the olfactory system's processing of multiple odorants embedded in complex mixtures, where perceptual interactions occur and support configural odor mixture perception. As a result, predicting the perceptual outcome of complex odor mixtures remains a significant challenge. This presentation introduces an innovative modeling approach integrating odor-active compound stimulus composition with expert knowledge to predict the odor quality of mixtures containing dozens of odorants. The model incorporates three types of heterogeneous data: chemical data, sensory data, and expert knowledge from flavorists. Expert knowledge is structured through an ontology and formalized using fuzzy rules optimized by an evolutionary algorithm. The model combines information from the odorants with the fuzzy rules to predict the mixture's odor profile, including both odor quality and intensity. This model was successfully applied to red wines, where the odor profiles were predicted based on Gas-Chromatography-Olfactometry analyses of their composition. Overall, this presentation highlights novel approaches to understanding odor quality construction in complex odorant mixtures. This work was supported by the Agence Nationale de la Recherche (ANR-18-CE21-0006 MULTIMIX) and the Conseil Régional Bourgogne, Franche-Comté (PARI-2015).

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

12:30 - 2:00 PM	Calusa ABC
The Barry Davis Funding Workshop for New Investigators	

This workshop will include an overview of research, training, and funding opportunities for graduate students, postdoctoral fellows, and early stage investigators. The discussion will provide practical information on how grant applications are processed within NIH/NIDCD, including Institute and study section assignments, the peer review process, Advisory Council activities, pay lines, and the roles of program and review staff.

Chair(s): Nirupa Chaudhari and Diego Restrepo

2:00 - 4:00 PM	Calusa EFGH
Visceral and Sensory Signaling in Food Reward Valuation	

Chair(s): Janina Seubert & Geraldine Coppin

Merging The Two Roads-Current Insights On Integration Of Visceral And Sensory Signalling In Food Reward Valuation

Janina Seubert[1], Geraldine Coppin[2,3]

[1]Karolinska Institutet, Stockholm, Sweden, [2]Swiss Center for Affective Sciences, Geneva, Switzerland, [3]UniDistance Suisse, Geneva, Switzerland

In a world where high-caloric foods are available in excess and overconsumed by many, the factors that drive humans towards specific food rewards and away from others urgently require better understanding. Food preferences are known to be acquired over the life course through contingencies between the experience of their specific flavors and both their positive metabolic outcomes (flavor-nutrient learning) and their associations with previously liked sensory properties (flavor-flavor learning). While both processes are increasingly understood at the neural and behavioral levels, research on these two subfields of food reward learning remains somewhat poorly integrated, and the development of an overarching framework for the integration of visceral and sensory processing of food reward is still ongoing. Uniting these complementary perspectives is key to understanding the complex interplay between the formation of reward predictions which drive our cravings and food choices, and the potential overconsumption of food. This symposium aims to bring together leading experts on food reward valuation who tackle the problem from sensory and visceral viewpoints, and who relate behavioral findings to brain function to create mechanistic insights into regulatory processes.

Gustatory And Interoceptive Pathways Modulate Striatal Reward Circuits To Regulate Sugar Intake

Luis A Tellez[1], Rafael Sandoval-Rodrı´guez[1], Wenfei Han[2,3], Ivan E de Araujo[2,3]

[1]Institute of Neurobiology at UNAM, Queretaro, Mexico, [2] Icahn School of Medicine at Mount Sinai, New York, NY, United States, [3]Max Planck Institute for Biological Cybernetics, Tubingen, Germany

While carbohydrates play a crucial role in survival, their strong reinforcing properties contribute to the increasing rates of obesity and diabetes worldwide. These reinforcing properties operate through gustatory and post-ingestive pathways that stimulate brain reward systems regulating sugar intake. However, it remains unclear whether specific molecularly defined cells within the reward circuitry play distinct roles in initiating and terminating sugary meals. Using a rodent model in combination with cell-specific manipulations, behavioral tests, electrophysiological measurements, and optogenetic techniques, we show that two different types of dopamine receptor-expressing neurons in the ventral striatum have opposing effects on caloric sugar consumption. Specifically, medium spiny neurons (MSNs) that express D1 receptors promote sugar intake through specialized anatomical and functional connections with peripheral and central taste systems. In contrast, D2 MSNs were anatomical and functional linked to circuits that suppress appetite. Furthermore, optogenetic activation of D1 MSNs—but not D2 MSNs—during water licking was sufficient to mimic conditioned taste cues. On the other hand, D2 MSNs partially mediate the satiating effects of glucagon-like peptide 1 (GLP-1) agonists, and lesions in D2 neurons disrupt caloric regulation. Overall, our findings reveal a circuit-switch mechanism through which the striatal reward circuits regulate the initiation and termination of sugary meals. Our study enhances our understanding of the cellular and circuit mechanisms underlying sugar overconsumption.

Reliability-Dependent Integration Of Multisensory Flavor Signals By Gustatory Cortex Neurons

Joost X Maier, Isabella B Allar
Wake Forest School of Medicine, Winston Salem, NC, United States

Flavor is the quintessential multisensory experience, combining gustatory, retronasal olfactory and texture qualities to inform food perception and consumption behavior. However, the computations that govern

multisensory integration of flavor components and their underlying neural mechanisms remain elusive. Here, we use rats as a model system to test the hypothesis that taste and smell components of flavor are integrated in a reliability-dependent manner to inform hedonic judgments, and that this computation is performed by neurons in primary taste cortex. Using a series of two-bottle preference tests, we demonstrate that hedonic judgments of taste+smell mixtures are a weighted average of the component judgments and that the weight of the components depends on their relative reliability. Using extracellular recordings of single neuron spiking and local field potential activity in combination with decoding analysis, we reveal a correlate of this computation in gustatory cortex (GC). GC neurons weigh bimodal taste and smell inputs based on their reliability, with more reliable inputs contributing more strongly to taste+smell mixture responses. Input reliability was associated with less variable responses and stronger network-level synchronization in the gamma band. Together, our findings establish a quantitative framework for understanding hedonic multisensory flavor judgements and identify the neural computations that underlie them.

Metabolic Modulation Of Appetitive Odor Processing In Food Reward Valuation

Androula Savva[1,2], Marc Guitart-Masip[3,4,5], Ata Ghaderi[1], Cynthia M. Bulik[2,6,7], Janina Seubert[1]
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Hunger is a powerful motivational state that enhances both the hedonic value of food and the drive to pursue food rewards. In this state, sensory cues, particularly odors, play a key role in triggering anticipatory reward responses, motivating individuals to seek and consume food. Unlike visual or auditory cues, odors are uniquely effective in evoking memories of food and eliciting physiological responses that prepare the body for food intake. However, the specific mechanisms by which food odors invigorate reward-driven actions, and how these effects vary by metabolic state, remain poorly understood. In this study, we present a novel experimental paradigm that separates invigorating effects of food stimuli on reward-seeking behavior, across two sensory modalities. In a food incentive delay paradigm, participants completed a reaction time task in which they could earn points that were exchanged for snacks at the end of the study. Participants (N=48) attended two experimental sessions after an overnight fast and completed the study once while hungry and once after consuming a standardized ad libitum breakfast. Prior to each trial (rewarded, non-rewarded), participants were presented with either an odor or a picture (food, non-food) and were instructed to press a button as soon as a symbol appeared on the screen. Our results indicate that hunger selectively improves reward-seeking performance when the task is preceded by a food odor, but not a food picture. Additionally, food and non-food stimuli elicit no differentiable invigorating effects on reward-seeking behavior in a satiated state. Taken together, these findings highlight the distinct role of odors in driving reward-seeking behavior in hunger and open up unique avenues of investigation into populations with maladaptive eating behaviors.

How Sleep Patterns Impact Chemosensory Processing And Eating Behaviors

Surabhi Bhutani
San Diego State University, San Diego, CA, United States

Obesity affects 42.5% of U.S. adults, posing a significant burden on the nation's health and escalating medical costs. Epidemiological and experimental studies have consistently linked unhealthy sleep patterns to an increased risk of obesity, partly due to their impact on the increased consumption of energy-dense, poor-quality foods. Smell and taste, which play critical roles in shaping food choices and eating patterns, may serve as key mediators in this relationship. But how do sleep attributes (quality, duration, timing, etc.) influence chemosensory perceptions? I will present findings from past and ongoing studies that explore the intersection of sleep, chemosensory function, and dietary behaviors. I will share our research demonstrating that variations in sleep duration and timing are associated with changes in olfactory perception and dietary preferences, particularly for energy-dense foods. Additionally, I will examine how unhealthy sleep patterns impair taste hedonic evaluation (e.g., liking and preference), further reinforcing unhealthy food choices. Together, these findings will provide valuable insights into the complex interplay between sleep, smell, taste, and dietary behaviors, with important implications for obesity prevention strategies.

How Do Sound And Light Cues Alter Motivation For Risky Gambles?

Catharine A. Winstanley
University of British Columbia, Vancouver, BC, Canada

It has long been known that audiovisual cues, when paired repeatedly with appetitive outcomes like sugary rewards or liquids, can come to act as reinforcers in their own right due to the attribution of incentive salience. Electronic gambling machines and gaming apps make heavy use of these cues to signal rewarding events during play. We have shown that, in both rats and humans, presenting sound and light cues concurrent with reward delivery can increase preference for "high-risk, high-reward" options in laboratory-based gambling tasks. However, computational modeling using reinforcement learning algorithms suggest that cue-induced risky choice is not driven by enhanced learning from rewards, as we would expect if the cues were acting as conditioned reinforcers, but instead through impaired learning from penalties. Furthermore, analyses of data

from over 800 rats suggest that even though the risk-promoting effect of the cues looks superficially similar across sex, cue-induced risky choice may operate via different cognitive processes in females vs males. Data from behavioral pharmacology studies and chemogenetic manipulations suggest reward-concurrent cues alter the recruitment of multiple neurotransmitter systems and brain regions in the decision-making process. Although daunting in its complexity, these studies also suggest a variety of approaches that may neutralize the deleterious effect of such cues on cognition.

2:00 - 4:00 PM	Calusa ABC
Emerging therapeutics for olfactory dysfunction	

Chair(s): Kai Zhao

Emerging Therapeutics For Olfactory Dysfunction
Kai Zhao
Department of Otolaryngology, Head&Neck Surgery, The Ohio State University, Columbus, OH, United States

The COVID-19 pandemic has left millions of new patients with olfactory dysfunction. Responding to this broad and urgent public health concern, the frontiers in therapeutics for olfactory dysfunction are as novel and exciting now as they have ever been, with a surge of new clinical trials/studies. In this symposium, we summarize and discuss latest therapeutics and clinical trials for olfactory disorders: from the established pillars of olfactory training and corticosteroids, to the use of supplements, biologicals, topical medications, neuromodulators, nerve block, platelet-rich plasma, as well as electric stimulation and non-invasive smell aids. This symposium targets not only clinicians, but also basic scientists interested in translational research, and aims to build new connections between basic researchers and frontline clinicians.

Inflammation And Olfaction: What&Rsquo;S The Link?
Justin Turner
University of Alabama at Birmingham, Birmingham, AL, United States

Inflammation can have both short- and long-term impacts on olfactory function in humans. Here we will review current scientific and clinical evidence related to the role of inflammation in olfaction, including potential mechanisms through which specific inflammatory mediators can have lasting effects on the olfactory epithelium. Current understanding of inflammatory disease processes that affect olfaction will be reviewed along with associated therapeutic approaches that can directly or indirectly improve olfactory function.

Emerging Therapies For Olfactory Dysfunction: From Preclinical Studies To Randomized Controlled Trials
Carol Yan
University of California San Diego, San Diego, CA, United States

Olfactory dysfunction (OD) affects millions globally, significantly impairing quality of life. Despite its prevalence, effective therapies remain limited. This presentation explores novel therapeutic strategies for OD, spanning preclinical research to randomized controlled trials (RCTs). Mechanistic studies have identified upregulation of pro-inflammatory and immune pathways in the olfactory epithelium following viral infections, contributing to persistent OD. Interferon-gamma (IFN-γ) has been implicated in this inflammatory response, with increased expression observed in the olfactory epithelium of patients experiencing post-viral OD. Olfactory training, leveraging neuroplasticity, continues to show efficacy in improving olfactory function across etiologies, including post-viral OD. Topical medications including corticosteroids and dietary supplements such as omega-3 and alpha lipoic acid are being investigated for their anti-inflammatory and neuroregenerative properties in RCTs. Platelet-rich plasma (PRP) injections has emerged as a promising intervention, demonstrating potential to modulate the olfactory microenvironment, enhance neurogenesis, and reduce inflammation in preclinical models and early clinical studies. A recent systematic review and meta-analysis suggested that PRP injections into the olfactory cleft may be effective in patients with persistent OD. Ongoing studies are investigating the utility of PRP injections for treating qualitative OD such as parosmia. Further mechanistic studies, standardized protocols, and larger trials will help validate these therapies and identify optimal patient candidates.

The Future Of Treating Smell Loss
Zara M. Patel
Stanford University School of Medicine, Stanford, CA, United States

As part of this panel, the audience will have heard from one of our colleagues already of our work using platelet-rich plasma (PRP) injections to treat post-viral smell loss. In this talk, we will cover the most recently published study examining the long term follow up outcomes with PRP one year after the original randomized controlled trial, and explore potential uses in other etiologies of smell loss. Additionally, we will discuss our randomized controlled trial investigating omega-3 as a treatment option for smell loss after surgery, and discuss potential use in other etiologies of smell loss. Finally, we will discuss our current research exploring both endoscopic electrical recording from the olfactory epithelium in humans, as well as endoscopic electrical stimulation, and why this may be the future of treatment for patients suffering from smell and taste loss, as well as other associated neurodegenerative diseases.

The Use Of Neuromodulators To Improve Parosmia After Covid-19 Infection
Do Yeon Cho
University of Alabama at Birmingham, Birmingham, AL, United States

Introduction: Post-viral olfactory dysfunction (PVOD) has risen dramatically since the COVID-19 pandemic. Parosmia, often described as a foul or rotten odor, can significantly impact the quality of life, as patients struggle to tolerate previously pleasant scents. This condition persists long-term, with recent studies reporting a 25-43.2% incidence of parosmia six months post-infection. This study aimed to evaluate the therapeutic potential of gabapentin for parosmia following COVID-19. Methods: Medical records of patients from the Smell and Taste

Clinic were reviewed. The University of Pennsylvania Smell Identification Test (UPSIT) identified olfactory dysfunction (OD), and parosmia was determined through patient history. Inclusion criteria were parosmia and at least six months of OD with abnormal UPSIT scores. Gabapentin treatment began at 100 mg daily for one week, increasing to 200 mg daily the following week. Dosage was adjusted weekly by 100-300 mg based on tolerance and symptom improvement, up to 600 mg daily. Phone interviews assessed outcomes at the maximal tolerable dosage (MTD) after a minimum of three weeks. Results: Of 85 PVOD patients evaluated over six months, 14 (16.5%, male-to-female=1:13, mean age 41.2 years) reported parosmia as a primary complaint (mean pre-treatment UPSIT=20.9±7.5). Gabapentin was prescribed to 12 patients; two postponed treatment. Of the remaining 12, two were discontinued due to drowsiness, and one was excluded for insufficient treatment duration. Among nine patients completing >3 weeks at MTD, eight (88.9%) reported improvement, including six (66.7%) with foul-smelling parosmia who showed significant improvement. Conclusions:
Gabapentin demonstrates potential as a well-tolerated treatment for parosmia in COVID-19 patients.

Designing Non-Invasive Smell Aids To Improve Olfactory Function In Patients With Broad Etiologies Including Long Covid: A Clinical Trial.

Veronica L. Formanek, Barak M. Spector, Gabriela Zappitelli, Zhenxing Wu, Kai Zhao
Department of Otolaryngology - Head & Neck Surgery, The Ohio State University, Columbus, OH, United States

Eyeglasses, hearing aids, etc. serve to enhance the external sensory stimuli to enable patients to see or hear things that they wouldn't otherwise be able to, but we have no equivalent technology for olfaction, in the direr post-COVID era. We attempt to invent "Smell-Aids" by enhancing intranasal odorant delivery to the olfactory epithelium, using two prototypes: (a) a nasal foam plug with a diagonal channel embedded that would direct air/odor flow upwards to the olfactory region; (b) a clip pinching a critical nasal valve region that may intensify the nasal airflow vortex to the olfactory region; and tested them on 54 patients with confirmed olfactory losses (age 21-80y, median 54.5). Majority (37/54=69%) were post-COVID long haulers (infected 12/15/2019 to 10/4/23; persisted 30 to 1260 days, median 22 months), while non-COVID smell losses (n=17) span from 5m-27 years (median 8.5 y). The 9-item NIH toolbox odor ID score significantly improved after application of both smell aids (in counter-balanced order, baseline: 4.30±2.27, pinch 4.82±2.06, plug 5.11±2.32, mixed model $p<0.05$), especially among the non-COVID cohort. For COVID long haulers, only the nasal plug showed significant improvement ($p<0.05$). The confidence score among both cohorts significantly improved with the nasal plug but not the pinch prototype. Further subgroup analysis on patients who reported diminished (hyposmia/anosmia 38/54) vs distorted smell (parosmia/phantosmia 27/54, n=11 reported both) showed that the nasal plug remains effective for both cohorts, while the pinch is only effective for the hypo/anosmia cohort. These results preliminarily demonstrated the potential to improve olfactory function through different peripheral mechanisms for different patient cohorts and may one day lead to an effective OTC smell aid.

101 **Mice Can Condition Insulin Release To The Sensory Properties Of Chow Diets**

Laura Mittelman, Natalie Ashkar, Fatima Khwaja, Clara Resnick, John I. Glendinning
Barnard College, Columbia University, New York, NY, United States

The pre-absorptive secretion of insulin, known as the cephalic-phase insulin response (CPIR), is triggered by the sensory features of fluids and foods. It enables mammals to limit postprandial elevations in blood glucose. We determined previously that fluids containing free glucose can reliably elicit a CPIR in C57BL/6 (B6) mice that are naïve to glucose or other pure carbohydrate solutions. Our new project asked whether B6 mice generate a CPIR when chewing chow diets. First, we found that hungry B6 mice reliably generate a CPIR after 15 s of chewing a familiar chow pellet, and that the CPIR was not associated with any elevation in blood glucose. Second, we asked whether this diet-induced CPIR requires conditioning. To this end, we tested two types of chow (standard and purified), which had a similar macronutrient composition, but differed in appearance, texture, taste and odor (according to human observers). We found that mice raised on standard chow generated a CPIR when chewing standard chow but not purified chow. In contrast, mice raised on purified chow generated a CPIR when chewing purified chow but not standard chow. It follows that B6 mice conditioned a CPIR to the unique sensory properties of each type of chow. Third, we observed that 4 weeks of continuous exposure was required to induce a CPIR to each type of chow. Fourth, we examined the necessity of olfaction to the diet-induced CPIRs. We impaired olfaction by treating mice with intranasal $ZnSO_4$. We found that $ZnSO_4$-treatment eliminated the conditioned CPIR to standard chow but not purified chow. We conclude that (i) B6 mice can condition CPIRs to specific chow diets, (ii) the conditioning takes about 4 weeks, and (iii) the relative importance of olfaction to the conditioned stimulus varies across diets.

103 **Digging For Dinner: Exploring How Internal And External Chemical Cues Modulate The Feeding Behavior Of Earthworms.**

Rebeca V Rodriguez[1], Folashaye E Araromi[2], Jonathan G Mebrahtu[2], Ameena A Mohassib[2], Laura Ortega-Damian[2], Diana M Quiroz-Ruiz[2], Tania C Romero[2], Renalison Farias-Pereira[1,2], Maria A Shumskaya[1,2], Mingjing Sun[3], Cecil J Saunders[1,2]

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The feeding behavior of animals is influenced by both internal and external chemical signals. Earthworms are detritivores that extract nutrients from the decaying organic component of soil. Ecological studies have indicated that earthworms are attracted to soil containing higher amounts of decaying organic material. While these previous studies have not attempted to specify individual molecules that alter the feeding behavior of earthworms, our experiments on the European nightcrawler (*Dendrobaena veneta*) have indicated that one such chemical signal is free amino acids. Specifically, we have observed that adding solutions of 50 μM to 100 mM L-Glutamic acid (ANOVA $F[1,381]=6.971$, $p<0.01$) and L-Alanine (Pairwise T-test, adj-$p<0.001$, $n = 21$) to soil significantly alters the soil feeding rate, while Glycine does not. To validate these experiments, we are currently determining and confirming the quantity and type of free amino acids in control and experimental soil using a Waters LCMS Quadrupole time-of-flight system. We have also collected data supporting the hypothesis that changes in an earthworm's internal metabolic state caused by starvation bouts of 5 to 30 days will significantly increase the feeding rate (ANOVA $F[1,38]=9.09$, $p<0.01$). To confirm these starvation bouts are sufficient to induce metabolic changes indicative of starvation, we have measured significant decreases in tissue glucose & trehalose ($p<0.05$, $n =9$), triglycerides ($p<0.05$, $n =9$), and total protein (T-test $p<0.01$, $n =9$) between 14 and 28 days. Taken together, these results suggest that free amino acids are likely one of the chemical signals that attract hungry earthworms to soils containing more decaying organic material.

105 **Pharmacological Activation Of An Extra-Oral Bitter Taste Receptor Modulates Both Metabolic And Senotherapeutic Pathways Providing The Opportunity To Treat Diseases Of Aging Via A Single Therapeutic Target**

J. Michael French[1], Allancer Nunes[2], Bernard P. Kok[3], Anna Carey[2], Andrea Galmozzi[3], Richard L.X. Ho[1], Christina D. Camell[2], Paul D. Robbins[2], Enrique Saez[3]

[1]Amaro Therapeutics, Inc., New York, NY, United States, [2]Masonic Institute on the Biology of Aging and Metabolism, University of Minnesota, Minneapolis, MN, United States, [3]Department of Molecular and Cellular Biology, The Scripps Research Institute, La Jolla, CA, United States

In these studies, we look to demonstrate the dual role of TAS2R1 in the treatment of obesity through regulation of both metabolic pathways and senescence cell signaling. Traditionally linked to taste perception, bitter taste receptors are G-protein coupled receptors that have recently emerged as regulators of metabolic and cellular processes in extra-oral tissues. TAS2R1, a human bitter taste receptor, and its mouse homolog Tas2r108, play a key role in metabolic regulation and cellular senescence. TAS2R1/r108 activation in the intestine remodels enteroendocrine hormone signaling, triggering secretion of gut hormones such as glucagon-like peptide 1 (GLP-1). Studies in obese-diabetic mice revealed that activation of intestinal Tas2r108 enhances glucose clearance, reduces fat mass, normalizes plasma lipid profiles, and quells systemic inflammation. These findings highlight

the potential to target TAS2R1/r108 to treat obesity and linked metabolic conditions. T Given that several natural products (e.g., fisetin, quercetin) with senotherapeutic activity, able to suppress or selectively kill pathogenic senescent cells that accumulate with age, have been shown to interact with bitter taste receptors, here we explored the role of bitter receptors in regulating senescence. Senescent cells, characterized by increased markers of cellular aging and senescence-associated secretory phenotypes (SASPs), show elevated TAS2R1/r108 expression. Activation of these receptors reduces markers of senescence and SASPs ($p16^{INK4a}$, $p21^{Cip}$, TNFa, IL6, IL1β, MMP-3), eases tissue inflammation and increases plasma levels of GLP-1 in aged mice. These effects are mediated through TAS2R1/r108-elicited PLCβ2 and IP3R signaling. Inhibition of these pathways attenuates the senotherapeutic effects of receptor activation. The dual roles of TAS2R1/r108 stress its potential as a target for obesity, diabetes, and age-associated conditions. Further research into the tissue-specific roles of TAS2R1/r108 holds promise for advancing therapeutic strategies that integrate metabolic and anti-senescence interventions.

107 **Semaglutide Decreases Hedonic Eating In Female Rats With A History Of Binge Eating.**

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

Semaglutide (SEMA) is effective in decreasing caloric intake, leading to weight loss in individuals with obesity. Less is known about its ability to decrease binge eating in individuals with bulimic syndromes. Here, we tested the hypothesis that SEMA would decrease the overconsumption of calories in a rodent model of binge-like eating. To induce binge eating, female rats were maintained on chow and given intermittent access to high fat diet (HFD) at 4-day intervals (INT group). Control groups had free access to chow or chow and HFD (CHOW and HFD groups). Within these diet groups, rats received daily injections of SEMA (70 mg/kg) or vehicle. We further assessed SEMA's ability to decrease hedonic eating in a 30-min chocolate Ensure "dessert" test, administered immediately after the consumption of a satiating meal. During the binge eating phase of the study, SEMA decreased cumulative food intake in INT and HFD groups, but not the CHOW group. When HFD was available, INT rats consumed 30-40% more calories than control groups (i.e., binged) during the first 2h of the dark phase. SEMA suppressed caloric intake during this 2-h period by ~20% in INT animals, but had no impact on food intake in HFD or CHOW animals at this timepoint. During the dessert test, SEMA decreased chocolate Ensure intake by 20-25% in INT rats but had no effect in CHOW or HFD rats. SEMA was also more effective in decreasing fat mass by over 50% (assessed via EchoMRI) in HFD and INT rats, but not CHOW rats We conclude that SEMA decreases hedonic eating in female rats with prior, intermittent exposure to HFD. Ongoing analyses are examining whether these effects of SEMA are mediated by its ability to increase meal-stimulated satiation signals.

109 **Loss Of E2 In Female Rats Promotes Greater Dysregulation In Body Weight And Feeding Behavior Than Exposure To An Obesogenic Diet.**

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Diet-induced obesity (DIO) is studied primarily in male rodents, with a limited literature in females suggesting that they are less susceptible to DIO than males. While the inhibitory effect of estradiol (E2) on chow intake is well established, less is known about its ability to reduce hedonic eating, which could protect against DIO. In the current study, food intake (45% high fat diet (HFD) or chow) and body weight were monitored for 4 weeks in ovarian-intact (INT) and ovariectomized (OVX) rats with or without E2 replacement. In an acute test of hedonic eating, rats were given 30-min access to chocolate Ensure "dessert" immediately after consuming a satiating test meal. Sucrose intake was then assessed in all groups using a series of two-bottle preference tests (ascending concentrations of sucrose vs. water). Loss of E2 promoted greater weight gain than having access to HFD (i.e., 4-week weight gain in OVX-oil-chow rats > INT-HFD and OVX-E2-HFD rats). Among chow-fed rats, the OVX-oil group consumed more chocolate Ensure "dessert" than OVX-EB and INT rats, but this effect was not seen in HFD-fed rats. Preference for sucrose was not influenced by diet or E2. These findings demonstrate that loss of E2 promotes greater body weight dysregulation than the consumption of an obesogenic diet and that this effect may be mediated by E2's ability to decrease hedonic eating. Ongoing studies are exploring how neuroinflammation, impaired response to satiation signals, and changes in taste bud number contribute to impaired weight regulation in chow-fed OVX rats, and how E2 may protect against these changes.

111 **Reports Of Smell And Taste Adverse Events From Glp-1 Ra&Rsquo;S**

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Background: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are widely prescribed for treating type 2 diabetes and obesity by regulating appetite, a function heavily influenced by taste and smell. Post-marketing surveillance data from the FDA Adverse Event (AE) Reporting System was used to evaluate the effects of GLP-1 RAs on taste and smell. Methods: We analyzed AE reports (01/01/2019–09/30/2024) on taste disorders (dysgeusia, ageusia, hypogeusia, non-specified taste disorder) and smell disorders (anosmia, hyposmia, parosmia, phantosmia) for GLP-1 RAs (semaglutide, dulaglutide, exenatide, liraglutide, lixisenatide; N=113,452) and non-GLP-1 RA drugs with known chemosensory adverse effects [i.e., metformin (non-GLP-1 RA drug for diabetes), nirmatrelvir (Paxlovid), and terbinafine (antifungal); N=257,356] using a standard disproportionality approach. Results: As expected, non-GLP-1 RA drugs exhibited high (>2.0) Reporting Odds Ratios (ROR) for

one or more chemosensory AEs, with the largest effects for taste dysfunction. Examples include metformin for parosmia (ROR=4.8; 95% CI 3.8-6.0), nirmatrelvir for dysgeusia (ROR=83.0; 95% CI 80.3-85.7), and terbinafine for ageusia (ROR=39.0; 95% CI 32.8-46.3). Although GLP-1 RAs overall demonstrated high associations among non-specified taste disorders (ROR=2.1; 95% CI 1.9-2.3) and parosmia (ROR=2.5; 95% CI 2.0-3.1), these effects are lower than observed for the non-GLP-1 RA drugs. Among GLP-1 RAs, semaglutide demonstrates the strongest associations, with an ROR=3.6 [95% CI 3.2-4.1] for taste disorder and ROR=4.4 [95% CI 3.3-5.8] for parosmia. Conclusion: GLP-1 RAs show significant associations with taste and smell disorders, the nature of which requires further study.

113 **Hacking Behavior: Maintenance And Modification Of The Davis Rig Platform**

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The Davis Rig platform has been established for decades as the premier brief-access task (BAT) for the testing of ingestive behavior. During this period, the hardware has remained largely unchanged, mainly because it is quite robust. In the meantime, however, computer technology has advanced considerably, and software/firmware support for the platform has lagged behind. The consequences of this are twofold: 1) the capabilities and flexibility of the Davis Rig has been limited by the software, artificially constraining the scope of experiments; and 2) computer senescence has tended to orphan Davis Rig systems, leaving hardware with years of usable life to gather dust. Here, we attempt to remedy those concerns. By reverse-engineering Davis Rig function, we have set up the basis for open-source maintenance and modification of Davis Rig hardware. This includes independent hardware and software components. We describe a PCB adapter designed to facilitate resurrection of orphaned hardware, and also produce TTL event signals that can be exported to other devices. Additionally, we have developed a suite of open-source Python programs designed to allow enhanced control over the Davis Rig from either Windows or Linux systems, including over USB connection. These programs include a GUI interface for calibration of the hardware, the ability to control cameras and LEDs, and a simplified system for designing protocols, including the ability to limit trials by either lick duration or lick count interchangeably. We also describe a BAT apparatus that functions similarly to a Davis Rig, but uses photobeam lick detection rather than capacitive touch sensing, rendering it compatible with electrophysiology while maintaining all of the benefits of open-source programming described above.

115 **Intra-Oral Infusion Or Esophageal Gavage Of A Sucrose Solution Activates Similar Neuron Populations Throughout The Brain Of B6 Mice.**

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The orosensory and viscerosensory systems work together to regulate behavioral and physiological responses to eating and drinking. Many brain areas receive both orosensory and visceral input, however, the effect of these inputs on the number and distribution of active neurons throughout the brain is largely unappreciated. Therefore, we mapped neurons activated by intra-oral infusion (IO) or esophageal gavage (G) of 1.0 M sucrose in taste-related regions throughout the B6 mouse brain using Fos immunohistochemistry. The number and location of Fos-immunoreactive (Fos-IR) neurons elicited by IO (orosensory and visceral input) and G (visceral input) were very similar. When comparing the two modes of delivery directly, IO tended to elicit more Fos-IR neurons in the gustatory brainstem than G, however the only places that contained significantly more labeled neurons following IO delivery were the central medial (CM) and external medial (EM) subareas as well as the waist region of the parabrachial nucleus (PBN; *ps*<0.05). When expressing the data as the percent of neurons within a particular subarea, again the only differences between IO and G were in the brainstem. Specifically, IO of sucrose elicited a higher percentage of labeled neurons in the ventral nucleus of the solitary tract (NST) as well as the CM, EM, and waist regions of the PBN while G shifted the number of Fos-IR neurons to the lateral NST and dorsolateral subarea of the PBN. There were no differences in the number and distribution of neurons activated by IO and G in the forebrain areas examined. The similarity in the number and location of neurons activated by orosensory and visceral inputs throughout the mouse brain suggests that these inputs are integrated in these areas to regulate feeding and other taste-related behaviors.

117 **On The Ph Of The Human Olfactory Mucus**

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Background: Intranasal mucus is considered to be significant for olfactory function. Although it already has been shown to contain thousands of different molecules, little is known on its basic physico-chemical characteristics. Objectives: The study aimed to determine the intranasal pH measurements of the mucus *in situ* at the respiratory and the olfactory mucosa, respectively. In addition, the relationship between pH and olfactory function was investigated. Methods: A total of 62 healthy, subjectively normosmic participants were included after they had been thoroughly explored with regard to their medical history, nasal anatomy (nasal endoscopy), and olfactory function (Snffin' Sticks odor identification [Odor_Id] test). pH-measurements (Restech Dx-pH; Respiratory Technology Corp., Houston, USA) were made at the respiratory mucosa (RM) at the lateral nasal

wall anterior to the middle turbinate and in the olfactory cleft (OC). Results: RM pH measurements (M_{27}=7.26±0.35) were significantly higher than OC pH (M_{35}=6.93±0.36; t_{60}=3.51, p<0.001). Odor identification scores correlated with OC pH (r_{35}=-0.43, p=0.01) but not with RM pH (r_{27}=-0.003, p=0.99). In an exploratory linear regression model, OC pH predicted 18% of the variance in Odor_Id scores & was a significant negative predictor of Odor_Id performance (as pH increases, Odor_Id decreases). Conclusion: The pH of the nasal mucus appears to be different in the respiratory and the olfactory mucosa, respectively. Higher acidity in the olfactory cleft was related to better olfactory function, suggesting that the nasal mucus may exert major influences on olfactory sensitivity, which deserves further study.

119 **Chemosensory Function And Psychological Factors In Chronic Nasal Obstruction**

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Chronic nasal obstruction (CNO) affects up to one-third of the population, with symptoms often inconsistent with anatomical findings or objective measurements. This study aimed to investigate the role of chemosensory function and psychological factors such as depression, anxiety, and stress in CNO. Literature suggests that trigeminal sensitivity, contributing to nasal airflow perception, and psychological factors like anxiety and depression significantly impact symptom perception and post-surgical outcomes in CNO. An ongoing prospective case-control study is conducted at a tertiary rhinology clinic with currently 115 participants (86 patients with CNO and 29 controls; M:F = 64:51; mean age 36.34 ± 12.7 years). Subjective nasal obstruction was assessed using NOSE and NO-VAS scales, while objective measurements included peak nasal inspiratory flow (PNIF) and anterior rhinomanometry (AR). Chemosensory tests comprised trigeminal sensitivity (lateralization test) and olfactory function (Sniffin' Sticks), alongside psychological evaluations via the Patients Health Questionnaire (PHQ) questionnaire. Results revealed no significant differences in objective nasal obstruction measurements or trigeminal sensitivity between groups. However, patients with CNO displayed significantly lower olfactory function and higher levels of depression and stress compared to controls. Subjective nasal obstruction strongly correlated with psychological factors, but not with objective measurements or trigeminal sensitivity. These findings suggest that CNO is multifactorial, with psychological variables playing a key role in symptom perception. Further investigation into anatomical and chemosensory contributions are vital in understanding CNO.

121 **Mucus-On-Chip: A Yeast-Olfactory Mucus Model System To Investigate The Impact Of The Mucus Layer On Odor Reception**

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Odor perception is a crucial aspect of human life. Odorant molecules are detected in the nasal cavity by olfactory receptors (ORs) on olfactory sensory neurons, which are covered with olfactory mucus. Olfactory mucus, 10–15 μm thick, has a thick periciliary liquid phase and a more viscous gel phase enriched with embedded mucins. It is composed of 90% water, mucins, ions, serum proteins, immunoglobulins, and lipids. It plays a vital role in trapping odorants and facilitating their interaction with ORs. Despite extensive OR studies, the interaction of aroma compounds with nasal mucus is still unclear. Lab-on-chip technology offers a novel platform to explore the role of mucus in odor detection. We aim to develop a 'mucus-on-chip' model by integrating humanized olfactory yeast biosensors into a two-phase microfluidic system to mimic nasal conditions. We engineered a yeast strain to express human OR, which fluoresces upon activation. N-terminal fusion with yeast α-factor secretion signal did not enhance OR expression or membrane localization in preliminary tests. For microfluidic fabrication, we selected thiol-ene polymers over PDMS due to its click chemistry properties. To mimic nasal mucus, we formulated polyethylene oxide (PEO)-based hydrogels. Early results show that PEO hydrogel viscosity increases from 0.008 to 0.05 Pa·s as concentration increases from 0.5% to 1.0%, exhibiting shear-thinning behavior akin to mucus. We are determining how pH, temperature, ions, sugars, and lipids affect viscosity and aroma diffusion. We are currently testing flow properties of different hydrogels in single-channel microfluidic device to optimize channel design. Once completed, this model will enable us to explore how mucus composition affects aroma compound diffusion and binding, ultimately advancing our understanding of olfactory mechanisms.

123 **Internal State Alters Dopamine And Serotonin Levels Prior To Sniffing In The Human Olfactory Mucosa**

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Olfaction is strongly modulated by internal state through poorly understood mechanisms. For example, during states of hunger, it is beneficial to respond to food odors attentively, whereas when sated, it could be beneficial to respond to food odors neutrally or with avoidance. In line with this, internal states of hunger enhance olfactory sensitivity, increase sniffing rates, and increase odor pleasantness ratings. Recent studies have made progress in understanding the role of central neural circuits in state-dependent control of olfaction. However, it is widely assumed that odor-induced signals make their way from olfactory sensory neurons (OSNs) to the brain unaltered. This assumption is at odds with the fact that in addition to odorant receptors, OSNs express receptors for many neuromodulators and are embedded in a bioactive mucosa that is extensively innervated. Thus, OSNs are poised

for state-dependent modulation. Here, we used human electrochemical methods to record sub-second dopamine and serotonin concentrations in the human olfactory mucosa during an olfactory satiety task. Our results show decreased dopamine levels in the nasal mucosa when participants were hungry compared to when they were sated, a result that is in line with the rodent literature. Further, we saw opponent dopamine and serotonin signaling that changed directions based on participants' hunger state, suggesting that dopamine and serotonin together may actually signal these state changes. These neurochemical changes were also accompanied by a moderate decrease in sniff inhales. Taken together, these results show that real-time neurochemical changes, at the level of the nasal mucosa in human participants, may be related to hunger state and subsequent inhalation profile.

125 **Inflammatory Modulation Of Olfactory Sensory Neurons And Immune Cells In The Main Olfactory Epithelium**

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The nasal epithelium, a frontline defense against foreign exposures, also contains the main olfactory epithelium (MOE)- the site of olfaction. MOE dysfunction, i.e. hyposmia or anosmia, significantly impacts quality of life. The MOE comprises multiple cell types, including olfactory sensory neurons (OSNs) and immune cells. Neuron-immune communication is likely critical, but how OSNs and immune cells interact in healthy and diseased states is a knowledge gap. During inflammation, OSNs must maintain olfactory function, then repair during recovery. We *hypothesized* that activated OSNs modulate local immune responses following inflammatory stimuli. Using single-cell RNA sequencing and flow cytometry, we identified OSNs, supporting epithelial, and immune cell subsets in dissociated MOE tissue. RNAseq identified differential gene expression in multiple cell types, including immune cells, after environmental olfactory exposures. Confocal microscopy showed resident immune cells in close proximity to OSNs, distributed across apical and basolateral regions of the epithelium. Following intranasal house dust mite extract (HDM) exposure for 7 days, however, did not significantly alter immune cell proportions in the MOE. Our findings indicate resident immune cells co-localize with OSNs and respond transcriptionally to environmental exposures. The lack of immune cell infiltration after acute intranasal allergic exposure suggests mechanisms to prevent excessive inflammation, potentially preserving olfactory function. Future studies will use live ex vivo and confocal microscopy to assess OSN activation and immune cell localization following HDM challenge.

127 **Encoding Of Odor Concentration By Neuronal Activity In Dorsal Ca1 In Mice Engaged In Odor Plume Navigation Is Dependent On Behavioral Context**

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Dorsal CA1 is likely involved in odor plume navigation because it is involved in spatial navigation and processes olfactory input from the lateral entorhinal cortex. We imaged dorsal CA1 pyramidal cells in Thy1-GCaMP6f mice using a miniscope and implanted GRIN lens. The mice performed odor plume navigation in a 50 x 48 cm^2 chamber with a steady 5 cm/s background air flow. When the mice reached the back of the chamber isoamyl acetate was released from one of two spouts located 5 cm from the side walls. The mouse was rewarded with water when it reached the odor release location. NoRMCorre was used for motion correction, and EXTRACT to find regions of interest (ROIs) with time-varying fluorescence signals reported as changes in fluorescence (DF/F) (Simoes de Souza et al, JoVE doi:10.3791/67039, 2024). We performed decoding of position and the logarithm of average odorant concentration using a binary decision-making machine learning algorithm. The algorithm was trained with z-normalized DF/F from all ROI activity using a leave one out approach. For position decoding there were no differences in the goodness of fit, quantified as the correlation (R1) between predicted and actual values, between hit and miss trials. In contrast, for prediction of odorant concentration R1 was higher for hits compared to misses and the highest correlation occurred after the mouse made a last turn towards the odorant. Interestingly, when ROIs were ranked in prediction importance the top 5% ROIs were largely nonoverlapping between prediction of position vs. odorant concentration. The data indicate that dorsal CA1 participates in combined computation of position and odorant concentration and that encoding of odorant concentration is dependent on behavioral context in odor plume navigation.

129 **Neural Dynamics In Gustatory Cortex During Taste Mixture-Based Perceptual Decision-Making**

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Gustatory cortex (GC) is crucial for mediating food-related behaviors, including taste-based decision-making, yet the functional role of GC dynamics in this context is still poorly understood. Here we analyze high-density electrophysiological recordings from GC neural ensembles in mice performing a sucrose/NaCl binary taste mixture-based decision-making task. Mice sampled a sucrose/NaCl mixture from a central spout, waited for a delay period, then licked a lateral spout for a water reward based on the predominant mixture component. We analyze each neuron's tuning curve over the time-course of a trial to classify it as *Linear* (continuous stimulus encoding), *Step-Perception* (categorical sweet/salty encoding), or *Step-Choice* (categorical left/right encoding). We find mostly Linear-coding units early in the trial, Step-Choice-coding units late in the trial, and a smaller number of Step-Perception-coding units throughout, suggesting a progression in coding from continuous stimulus to categorical perception and decision information over time. To investigate the genesis of these coding patterns and probe their functional significance, we train recurrent neural networks (RNNs) to perform the task while constraining them to reproduce the observed neural activity. We perturb the trained models by ablating sub-populations and find each type of coding unit, despite constituting a small fraction of the population, is necessary for normal task performance, while the remaining ~60% of neurons are not. In sum, our results suggest linear stimulus coding transitions into categorical coding of other task-relevant variables during taste mixture-based decision-making and highlight the importance of specific coding units for behavior.

131 **Contribution Of Olfactory-Driven Oscillations To Interbrain Synchrony In Socially Interacting Mice**

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Social interaction is essential for the well-being of individuals as well as for the functioning of societies. Social impairment manifests in neurodevelopmental and neuropsychiatric disorders. Social interaction involves extensive information exchange, behavioral coordination, and shared cognitive states between individuals. Remarkably, socially interacting brains exhibit some degree of coordination and synchronization, termed "interbrain synchrony", which may encode socially relevant information and enhance social interaction. Interbrain synchrony has been observed in the medial prefrontal cortex (mPFC), a key hub in social cognition. Meanwhile, respiration-entrained oscillations in the olfactory system are increasingly recognized as a powerful coordinator of neuronal activity in many brain areas, including the mPFC. However, the role of respiratory rhythms has not been considered in interbrain synchrony during social interaction. Here, we test the hypothesis that coordinated olfactory inputs among individuals in social settings contribute to interbrain synchrony via an olfactory-mPFC circuit. Local field potentials (LFPs) from the mPFC and olfactory bulb (OB) were simultaneously recorded from freely behaving pairs of mice. Neural synchrony was assessed by analyzing the correlation of the power spectrum within and between animals. The OBs of socially interacting mice showed increased synchrony relative to mice alone or not interacting, suggesting concurrently increased breathing frequencies. This pattern holds when evaluating the synchrony between mPFCs, and between the OB and mPFC within the same animal. We will investigate the interbrain synchrony profiles in socially impaired mice in the near future.

133 **A Pleasantness-Associated Receptor For A Key Odor Constituent Of Ambergris**

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Ambergris, a substance derived from the digestive system of sperm whales, has been valued for centuries for its unique aromatic properties. However, historical accounts indicate that certain human populations, particularly in East Asia, utilized ambergris without regard for its odor quality. These observations suggest that ambergris offers a model for studying regional variations in human olfactory perception. Despite its historical and cultural significance, the molecular basis of ambergris perception has remained unclear. In this study, we identified OR7A17 as an odorant receptor specifically tuned to (-)-Ambroxide, a key odorant in ambergris. Analysis of genetic and functional variations in OR7A17 revealed that non-functional alleles of this receptor are prevalent in human populations, particularly in East Asia. Individuals lacking functional OR7A17 alleles could still detect (-)-Ambroxide but found its scent less pleasant compared to those with functional alleles. These findings elucidate a molecular mechanism that influences the perceived pleasantness of ambergris and shed light on its enduring legacy in perfumery.

135 **Investigating The Mechanisms Of Multisensory Divided Attention In Humans**

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In complex natural environments, the ability to simultaneously attend to multiple sensory modalities and distinguish relevant information from irrelevant is essential for adaptive behavior. For example, making a decision about what to eat in a crowded street market may require attending to the sights, sounds, and smells of potential options. Divided attention tasks are an effective experimental model of multisensory processing. However, these tasks tend to utilize two modalities, and are typically limited to auditory and visual domains. The olfactory modality has received less focus in previous research despite being a significant part of daily sensory experience. Here we designed a study in which healthy participants (n = 50) experienced simultaneous presentation of odors, visual images, and sounds in a multisensory divided attention task. On each trial, prior to stimulus presentation, participants were cued to attend to one, two, or all three modalities, and then after stimulation probed on the specific identity of one of the attended modalities. We hypothesized that response time

would increase and identification accuracy would decrease with an increasing number of attended modalities in this task. Interestingly, we found that performance was significantly above chance in all attention conditions, with significantly decreased accuracy in any condition with olfactory attention. Additionally, the number of modalities attended did not have an impact on performance. These results indicate that humans have the capacity to simultaneously attend to auditory, visual, and olfactory information in multisensory conditions, with decreased accuracy for olfactory stimuli.

137 **Olfaction, Anxiety And Depression In Subjective Cognitive Decline**

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Olfactory dysfunction and neuropsychiatric symptoms such as anxiety and depression, are believed to be strong predictor of conversion from mild cognitive impairment (MCI) to Alzheimer Disease (AD). However, less is known about their occurrence in subjective cognitive decline (SCD), a preclinical stage of AD marked by self-reported memory complaints without objective cognitive impairments on standard neuropsychological tests. In this study we aimed to characterize olfactory function, anxiety, and depression, in individuals with SCD compared to controls. A total of 110 participants aged 60 and older were recruited, including 59 with SCD (42 women) and 51 healthy controls (35 women). Participants completed anxiety (GAI) and depression (GDS) questionnaires and underwent olfactory testing with the *Sniffin' Sticks* battery (threshold, discrimination, and identification). The SCD group exhibited significantly lower global olfactory performance (M = 31.1, SD = 7.0) than controls ($M = 33.6$, $SD = 4.7$), ($t(101.53) = 2.19$, $p = 0.03$)). Anxiety ($M = 3.3$, $SD = 3.7$) and depression ($M = 5.1$, $SD = 4.1$) scores were significantly higher in the SCD group compared to controls (anxiety: $M = 1.1$, $SD = 2.3$; depression: $M = 1.6$, $SD = 2.0$), with significant differences for both (anxiety: $t(97.59) = -3.46$, $p < 0.001$; depression: $t(88.80) = -5.86$, $p < 0.001$). No significant differences were found in specific olfactory submeasures. Combining global olfactory performance with anxiety and depression scores improved SCD status prediction and classification accuracy ($\chi^2(1) = 45.89$, $p < 0.001$).
These findings highlight subtle but significant and objective lower olfactory performance in individuals with SCD. Olfactory event related potentials should be explored to better understand possible underlying neurophysiological mechanisms.

139 **Concentration Dependence Of Conditioned Behavioral Response To Odorants In Newborn Rabbits**

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Newborn rabbits rely on olfaction to locate maternal nipples during the mother's single, brief daily visit to the nest. In their search for milk, they are predisposed to respond behaviorally to the mammary pheromone (MP; 2-methylbut-2-enal) emitted by lactating female rabbits. They also respond to maternal odor cues that they learned prenatally and/or postnatally. In particular, the MP itself promotes postnatal associative conditioning to novel (initially behaviorally inactive) stimuli in an extremely powerful way (single and brief episode of association): 24h after pairing with MP, neonates show typical head searching/oral grasping response to both the conditioned stimulus and the MP. Here, following a consistent study over more than two years and 300 pups, we tested whether the concentration at which an odorant is MP learned influences the range of concentrations to which the animals respond. We compared the post-learning orocephalic responsiveness of neonates to two odorants deliberately selected for high vs. low volatility. We will illustrate some of the results obtained for certain concentrations of conditioned stimuli (range: 10^{-3} - 10^{-24} g/ml), and the remarkable consistency (but not exact similarity) of the results obtained for the two odorants. The results reveal that i) generalization of odorant quality can occur after learning over a wide range of concentrations, but depending on the stimulus concentration at conditioning; ii) quality and intensity become closely dependent at the lowest concentrations. They highlight the remarkable adaptability of the neonatal olfactory system to the intensity of odors perceived in the environment, the formidable odor learning capacity of neonates, and raise questions about how olfaction actually works, especially under conditions of low concentration.

141 **Effects Of Odor-Evoked Taste-Specific Expectation On Gustatory Cortex Activity**

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The gustatory cortex (GC) plays a critical role in processing chemosensory information. Recent findings indicate that GC also encodes cognitive variables relevant to taste-related expectation and decision-making. Specifically, when non-taste sensory stimuli, such as odors or sounds, predict upcoming tastes, GC neurons exhibit outcome-specific, anticipatory responses to these cues. This type of activity enhances taste processing and influences ingestive behavior. However, the nature of the information conveyed by anticipatory GC activity, and how it guides behavior, remains unclear. To address this gap, we relied on a two-alternative choice task where two distinct odor cues instructed mice to lick, after a delay period, either a left or right spout, leading to a reward of either sucrose or monosodium glutamate (MSG) solution respectively. Preliminary experiments show that optogenetic inhibition of GC during this task increased the amount of lick direction errors, suggesting a role for GC in driving consumption decisions guided by olfactory cues. Using high-density probes, we examined GC

spiking activity during the period between odor presentation and taste sampling. We found anticipatory activity during the delay period in response to the different odor cues. To disambiguate if GC anticipatory activity reflected the expectation of lick direction or taste identity, another cohort of mice was trained on a task in which two additional odors also prompted left and right licks, but resulted in water delivery. Preliminary evidence demonstrates both direction-selective and identity-selective anticipatory activity during the delay period. Overall, these experiments highlight how the activity of GC neurons represents different aspects of taste expectation.

143 **Olfactory Discrimination Ability Is Associated With Behavioral Impulsivity In Patients With Borderline Personality Disorder**

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Previous studies have shown an overlap between the neural circuits involved in olfactory processing and behavioral regulation, such as response inhibition, with the orbitofrontal cortex playing a central role in both. An association between olfactory discrimination ability and behavioral impulsivity has also been reported in healthy participants.
In this study, we propose to investigate whether olfactory discrimination ability is related to behavioral impulsivity in a clinical psychiatric population, focusing on patients with borderline personality disorder (BPD), a condition characterized by emotional instability, risky impulsive behaviors, and orbitofrontal cortex dysfunction.
Seventeen patients were recruited for the study. Olfactory discrimination ability was assessed using a task consisting of 16 trials, each presenting 3 odorants (2 identical, 1 different). Participants were asked to identify the different odorant. Behavioral impulsivity was measured using a Stop Signal Task in which participants were instructed to respond quickly to a green cue and to withhold their response when a red cue appeared (25% of trials). The primary outcome was the Stop Signal Reaction Time (SSRT), which reflects the time needed to successfully inhibit a response. Longer SSRT indicate higher impulsivity.
Preliminary results showed a significant negative correlation between olfactory discrimination ability and SSRT ($r(16) = -.51$, $p = .036$), indicating that patients with lower olfactory discrimination abilities exhibited higher impulsivity.
These findings provide new insight into the relationship between olfactory discrimination deficits and neurocognitive functioning in patients with BPD, and may help identify patients most at risk for impulsive behaviors, including self-harm.

145 **Olfactory Identification Is Better To Rule Out Mild Cognitive Impairment Than Detecting It: Results From The Cima-Q Cohort.**

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Smell identification impairment is an early clinical marker of Alzheimer's disease (AD), already observable at the mild cognitive impairment (MCI) stage. Although olfactory identification is associated with episodic memory, its predictive power on cognitive performance remains questionable. This study aimed to (1) assess the predictive value of olfactory identification on episodic memory functioning, and (2) evaluate its role in distinguishing between individuals with MCI and those with subjective cognitive decline (SCD). We used the University of Pennsylvania Smell Identification Test (UPSIT) to assess smell function in 48 participants with SCD (mean age: 75.82, SD: 5.64) and 45 with MCI (mean age: 80.08, SD: 5.86) from the CIMA-Q cohort. Episodic memory was measured using the Rey Auditory Verbal Learning Test (RAVLT). LASSO regression models were applied, with 80% of the data used for training and 20% for testing. Group classification accuracy based on UPSIT scores was assessed with Linear Discriminant Analysis (LDA). UPSIT scores significantly correlated with both total (β=0.56,p<.001) and delayed recall (β=0.19,p<.001). Including UPSIT in predictive models increased the explained variance for total recall from 9% to 19% and delayed recall from 8% to 20%. The MCI group exhibited significantly lower UPSIT scores compared to the SCD group (p=.01); LDA demonstrated moderate accuracy (69%) in distinguishing groups, with higher specificity for ruling out MCI

(79%) than sensitivity for detecting it (58%). Olfactory identification enhances the prediction of episodic memory performance and shows potential as a screening tool for cognitive decline. As olfactory impairment is not specific to AD or MCI, higher scores on the UPSIT are more effective for ruling out MCI than low scores are for detecting it.

147 **Engagement Of Medial Prefrontal Cortex Circuitry To The Tubular Striatum During Olfactory Discrimination**

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The ability to attend to odors is critical for survival in animals including humans. The neural mechanisms that enable prioritization of odors, especially in complex sensory environments, remain unresolved. Previous work from our lab identified the tubular striatum (TuS) as the privileged recipient of inputs from the medial prefrontal cortex (mPFC). Specifically, the TuS receives inputs from subregions of the medial prefrontal cortex, including the orbitofrontal, prelimbic, and especially the infralimbic cortex. Given the mPFC's role in attention and the TuS's role in olfactory valence–dependent behaviors, we hypothesize that mPFC→TuS circuitry is important for olfactory attention. Using a combination of viral strategies, including GCaMP8 for calcium recordings and AAV1 for trans-synaptic Cre expression, we recorded activity of both mPFC neurons projecting to the TuS, and TuS neurons which received input from the mPFC. We shaped mice to perform a head-fixed lick-left/lick-right two-alternative forced choice odor discrimination task, which included air puff cues to alert the mice of upcoming odor delivery, and odors. Utilizing this approach, we discovered that mPFC→TuS circuitry is uniquely activated in several specific manners during olfactory behavior. First, the mPFC→TuS circuit is more greatly activated upon receipt of novel odors as well as unexpected non-olfactory cues. Moreover, distinct response patterns emerge when behavioral contingencies are reversed, reflecting the circuit's sensitivity to learned odor information. These initial findings suggest that the mPFC→TuS circuit multiplexes olfactory information with other sensory inputs and expectations, providing new insights into the neural mechanisms underlying the prioritization of odors.

149 **Local Field Potential Oscillations In The Olfactory-Limbic System Reflect Cognitive Load**

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Rat olfactory bulb (OB) local field potential (LFP) gamma (35–110 Hz) oscillations represent local network activity, and beta (15–30 Hz) activity is linked to systemwide engagement. Gamma band elevation during odor sampling is linked to the function of better fine (similar) odor discrimination. We investigate here the role of cognitive load and the associated LFP network states in driving increased gamma during an odor discrimination task. We used a variation of a 2-Alternative Choice (TAC) task in which higher cognitive load is achieved through an increased number of stimuli (4 instead of 2), highly similar odors (combinations of enantiomers), and low level of odor predictability. We used light cues to manipulate the predictability of the upcoming stimulus to affect discrimination difficulty. Male and female rats were implanted with LFP electrodes in the OB, anterior piriform cortex, and dorsal hippocampus (dentate gyrus[LK1] and CA1). Rats performed the TAC task with informative or non-informative cues. Manipulating the cognitive load for rats during this odor discrimination task affects rats' behavioral strategies and network LFP activity. The informative group performed slightly but significantly better, using a longer sampling duration but a shorter response time. OB gamma oscillations are modified in both groups during the waiting, cue, odor sampling, and response periods, differently for the two groups. The nature of the odor (fine vs. coarse) also modified gamma and beta power. Beta power was lower in all areas during fine, compared to coarse, discrimination, and in the OB beta power also depended on cue condition, learning phase, and test type. Cue condition also affected gamma and beta power in the hippocampus. We also show robust sex differences in both behavior and network activity.

151 **Smelling Healthy Choices: Exploring Neural Mechanisms Of Odor-Guided Food Choices**

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Healthy food choices are essential for health. While visual cues have been widely used to encourage healthier eating, olfactory cues represent a promising yet underexplored approach. Previous studies suggest that cognitive factors may play a role in how odors influence food choices. Investigating the underlying neural mechanisms of decision-making could further clarify these effects. We studied 30 participants, who made 120 food choices during fMRI scanning under three odor conditions: healthy odors (apple or cucumber), unhealthy odors (chocolate or chips), and a non-food control odor (rose). Each run consisted of 30 trials (10 per odor condition) and was repeated four times. In each trial, participants were exposed to an odor and then selected one food item they wanted to eat from four pictures (two healthy, two unhealthy) within 5.5 seconds. Behavioral data analysis using a linear mixed model revealed a main effect of odor on food choices ($\chi^2 = 125$, $p < 0.001$). The model analyzed the proportion of healthy choices (number of healthy choices divided by total choices) and showed that participants chose a higher proportion of healthy foods in the healthy odor ($M = 0.75$, $SD = 0.23$) and control odor condition ($M = 0.63$, $SD = 0.24$) compared to the unhealthy odor condition ($M = 0.18$, $SD = 0.23$), though no significant difference was observed between the healthy and control odor conditions. These results suggest that olfactory cues can influence food choices, with unhealthy food odors decreasing the likelihood of healthy

food choices. Neuroimaging data analysis is ongoing, with a focus on activation in the dorsolateral prefrontal cortex (dlPFC) and the ventromedial prefrontal cortex (vmPFC), and will further elucidate the neural mechanisms underlying these effects.

153 **A Benchmark For Large Language Models In Predicting Odor Identity**

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Recent breakthroughs in deep learning for odorant identity prediction are opening new venues for the generation of new odors. Yet, these models can only predict percepts from a fixed vocabulary and fail to fully render the complexity of odor perception. The lack of large-scale olfactory datasets and standardized metrics for the quality of odor description limits our ability to train new deep learning models. We introduce a novel benchmark of over 14K molecules for evaluating generative models on both constrained and open-ended descriptions of molecular percepts. Our work addresses critical gaps in current evaluation methodologies for odor identity. We first show that existing evaluation criteria, such as AUROC, are inadequate measures for olfactory descriptions and are unable to distinguish between human written descriptions across molecules. To address this limitation, we propose a model-based approach where pretrained Sentence-BERT models are finetuned on olfactory descriptions via contrastive learning objectives, significantly improving separability between human descriptions across molecules. We then show, using classical methods such as k-first retrieval tasks, that general purpose pretrained large language models (LLMs), lack the required domain knowledge for describing olfactory perceptions. To address this limitation, we introduce CIRANO, the first olfactory LLM that is trained using a custom-generated olfactory dataset of 100,000 molecules. Overall, our benchmark provides a standardized framework for evaluating computational models of molecular perception, offering insights into both the capabilities and limitations of current approaches while establishing a foundation for future research in molecular perception modeling and evaluation methodologies.

155 **The Pupillary Respiratory-Phase Response: Pupil Size Is Smallest Around Inhalation Onset And Largest During Exhalation**

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Respiration profoundly influences brain activity, coordinating sensory processing and motor actions. However, its effect on pupil size, a critical indicator of visual perception and neural state, remains underexplored. In five experiments using a pre-registered protocol—we systematically investigated how respiratory phase affects pupil size across different conditions. In Experiment 1 (n = 50), we examined nasal and oral breathing at rest under dim lighting with nearby fixation points and discovered that pupil size fluctuates with the respiratory cycle, being smallest around inhalation onset and largest during exhalation. These results were replicated in Experiment 2 (n = 53) using an independent sample under identical conditions. Experiment 3 (n = 112) demonstrated that this pattern persists during active visual tasks, while Experiment 4 (n = 57) showed it remains robust under controlled breathing at varying paces under ambient lighting and distant fixation. Finally, in Experiment 5 (n = 34) individuals with isolated congenital anosmia (born without olfactory bulbs) were used as a lesion-type model during visual-auditory tasks to assess whether the respiratory-pupil link depends on olfactory bulb-driven oscillations. The results were consistent across all conditions and groups, indicating that the Pupillary Respiratory-Phase (PRP) response is independent of breathing route, task, or olfactory bulb function. We propose that the PRP response is governed by brainstem circuits, involving the preBötzinger complex and locus coeruleus, which modulate pupil size in synchrony with respiratory rhythms. This novel mechanism complements the three established drivers of pupil size—light, near fixation, and psychosensory responses—by introducing a cyclic modulation tied to the respiratory phase.

157 **Rats Subjectively Weigh Multiple Reward Dimensions In A Free Taste Foraging Task**

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In the real-world, animals actively gather information about their environment. Actively sampling sensory signals enhances the ability to learn and make optimal decisions. However, the mechanisms underlying this process are poorly understood. Here, we address this issue using a two-alternative free choice taste foraging task in rats. In this task, rats sampled freely from two options that predicted delivery of different taste outcomes (sucrose, quinine, water) with varying probabilities. Option-outcome contingencies were stable within daily 1-hour long sessions but varied from day to day. The results show that rats dynamically sample among the different options. Over time within 1-hour long session, animals learned to maximize sucrose and minimize quinine intake, in a manner that was highly similar between individuals. However, individual animals behaved in unique ways when weighing different reward dimensions. These findings suggest that animals use the objective outcomes of previous choices to adapt subsequent choices to the reward structure of the environment, but that valuation of different choice outcome dimensions is highly subjective. Computational modeling of choice behavior shows that outcome value can be well-described by temporal difference reinforcement learning. Ongoing work aims to link dynamic changes in outcome value to neural responses in gustatory cortex.

159 **Modulating Odor Valence And Tolerability Through Non-Invasive Transcranial Focused Ultrasound Stimulation (Tfus) Of The Amygdala**

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Parosmia, a distorted sense of smell characterized by intense odor unpleasantness and disgust, affects a significant portion of people with COVID-related persistent smell dysfunction. Yet very little is known about parosmia, especially regarding its treatment. Previous animal studies suggest amygdala involvement in the processing of perceived odor valence. Transcranial focused ultrasound stimulation (tFUS) allows a safe and effective method for the precise stimulation of deep brain structures (e.g. amygdala), modulating neural circuits that were previously elusive to other more superficial stimulation methods like trigeminal nerve stimulation. The present study aimed to determine whether tFUS to the amygdala could modulate perceived valence and tolerability of odors. Ten normosmic adults provided baseline ratings of intensity, valence, and tolerability for a series of pleasant, neutral and unpleasant odors. Next, a structural MRI was performed to calculate the unique triangulation (i.e. coordinates) of the right amygdala. Participants returned to the study site for 2 follow-up visits during which they received counterbalanced, double-blinded administration of active or sham tFUS, and then provided ratings for the same odors. A significant effect of stimulation condition was demonstrated for perceived odor valence ($F(2,117)=4\ .415$, $p=.014$) and tolerability ($F(2,117)=3.828$, $p=.025$), but not odor intensity ($p>.1$). The odors rated most unpleasant at baseline were rated significantly more pleasant and tolerable after active, but not sham, stimulation. While preliminary and focused on one target (i.e. right amygdala), these findings show promise for tFUS as a tool to probe the olfactory circuit in humans. These data support further study of tFUS as a potential treatment intervention for parosmia as well.

161 **Investigating The Neural Basis Of Representation-Mediated Learning In Humans**

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The representation-mediated learning (RML) task has been used in rodents to demonstrate that mental representation of chemosensory stimuli can form associations with aversive stimuli, even if the chemosensory stimulus is not physically present. This behavioral effect is amplified in animal models of the positive symptoms of schizophrenia, suggesting that RML holds promise for identifying neural biomarkers of psychosis. We recently developed a human behavioral version of the RML task by showing that expected, but not delivered, odors can form associations with an aversive sound. In the current study, we aim to address the underlying brain mechanism by conducting an adapted RML task while participants undergo fMRI. Participants first learn associations between visual symbols and two distinct appetitive food odors. We then acquire pleasantness ratings for symbols and odors before and after one of the symbols is paired with an aversive sound. Preliminary results ($n = 9$) showed a selective decrease in pleasantness for the odor previously paired with the aversively conditioned symbol, similar to our previous study. Multivoxel pattern analysis of fMRI data indicate that mental representations of expected odors are embedded in distributed patterns of orbitofrontal cortex activity. Further planned analyses will test whether these mental representations are reactivated by the visual symbols during the aversive conditioning, and whether this predicts the propensity for odors to enter into association with the sound. Such findings may reveal novel targets for noninvasive stimulation-based treatments of psychotic symptoms.

163 **Modulation Of Taste Palatability By Grpr-Expressing Neurons In Mouse Gustatory Cortex**

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Eating is a multiphasic process that is directed by physiological and hedonic drivers responsible for the initiation, continuation, and termination of eating. The Gustatory Cortex (GC), as the primary cortical taste region, is a key player in mediating eating behavior. However, its role in meal termination remains elusive. Here we report that, in mice, GRP signaling through GRPR-expressing neurons in GC modulates taste palatability and, consequently, consumption. Using Conditioned Taste Aversion (CTA) we determined that GRP signaling through the GRP receptor (GRPR) is critical for de novo induction of aversive learning leading to diminished saccharine consumption. However, recall of learned association was not altered by GRP infusion. Our study suggests that the behavioral effects of GRP infusion depend on the recruitment of GRPR cells in the GC. Using whole cell patch clamp recording of ex vivo slices, we show that GRP application selectively increases excitability of GC GRPR expressing cells. Furthermore, GRP modulated synaptic inputs onto GRPR expressing cells, largely augmenting GABAergic tone. To garner a holistic understanding of the identity of the cells mediating these functional effects, we further characterize the heterogenous neurochemical and electrophysiological identity of GC GRPR expressing cells. These results point to a role for GRPR circuits in GC in the updating of hedonic value to innately appetitive tastants and more broadly point to a role for the recruitment of GRP-GRPR signaling in modulating the plasticity of palatability.

165 **Temporal Dynamics Of Decision-Predicting Time Cells In Olfactory Discrimination: Molecular And Neural Mechanisms Of Associative Learning**

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In nature, an animal's survival hinges on its ability to process and integrate sensory information. This skill is crucial for finding food, avoiding threats, and selecting mates. Importantly, the success of these behaviors is rooted in the interplay between olfaction and experience, especially influenced by available contextual information. Thus, simply detecting an odor is insufficient; an animal must apply meaning to it and respond appropriately. Previous research has consistently highlighted the hippocampus, particularly the dorsal CA1 (dCA1) region, as a key player in learning and memory processes. Our previous work has shown that during olfactory discrimination learning, dCA1 pyramidal cells develop specific responses to odors as animals become more adept at go/no-go tasks. Our recent findings reveal that certain groups of pyramidal neurons exhibit divergent responses to stimuli at specific time points, a phenomenon we term 'time tiling'. This can be conceptualized as a temporally distinct divergence in neural activity related to stimulus valence during the associative learning process of the go/no-go task, and thus we named these cells 'Decision Predicting Time Cells'or DPTCs. Utilizing two-photon microscopy, this work focuses on the molecular characterization of DPTCs, particularly their expression of Calbindin2, as well as the contribution of Parvalbumin interneurons to the go/no-go olfactory discrimination task. Ultimately this study will help to uncover crucial details about how memories are formed and retrieved in the brain, and through this work we expect to gain a deeper understanding of the neural mechanisms at play. Such knowledge could prove invaluable in unraveling the complexities of memory-related disorders and potentially pave the way for innovative therapeutic approaches.

167 **Stimulus Expectations Drive Conditioned Olfactory Hallucinations**

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Olfactory hallucinations represent a significant portion of experienced hallucinations in both clinical and healthy populations. Empirical studies of auditory and visual hallucinations have used Pavlovian conditioning paradigms to demonstrate that false perception is driven by overly robust representations of stimulus expectations. However, no study has established that a similar mechanism underlies olfactory hallucinations in humans. Here we implemented a conditioned olfactory hallucination paradigm in which we first determined the odor detection thresholds of butanol for each participant (n = 55) using an adaptive psychometric algorithm. Participants then completed an odor detection task where on each trial one of two distinct visual cues was paired with either a supra-threshold, threshold, or sub-threshold concentration of butanol, or no odor. In the first three blocks of task trials, one visual stimulus ("strong cue") was paired more frequently with supra-threshold concentrations, and the other visual stimulus ("weak cue") was paired more frequently with sub-threshold concentrations. In the last three blocks both cues were paired most frequently with the no odor condition. We found significantly greater odor detection rates on no odor trials for the strong cue compared to the weak cue ($t_{54} = 2.08$, $p = 0.043$). Importantly, this finding could not be explained by differences in total number of visual cue presentations or other task variables. We thus demonstrate that false odor perception can be enhanced by the expectation of an olfactory stimulus in a Pavlovian conditioning paradigm. Such findings could yield therapeutic insight into the mechanisms underlying pathological olfactory hallucinations.

169 **Decrease Expression Of CamkiiA Leads To A Change In Phase Amplitude Coupling (Pac) In The Go No Go Working Memory Task.**

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The alpha-isoform of calcium/calmodulin-dependent protein kinase II (CaMKIIα) plays a crucial role in brain function, with high expression in the hippocampus and prefrontal cortex. CaMKIIα is involved in various neurological processes and disorders, including synaptic plasticity, learning, memory, and cognition. Heterozygous CaMKIIα knockout mice (Het) exhibit developmental and behavioral abnormalities, such as hyperactivity and cognitive impairments. To delve deeper into CaMKIIα's role, we employed an olfactory working memory task to uncover cognitive learning deficits, coupled with awake behavior recording to gauge changes in neuronal oscillations in the hippocampus and prefrontal cortex. Mice adeptly associated odorants with water reward, and subsequent analysis revealed notable differences in Phase Amplitude Coupling (PAC) strength among wild-type (WT), Het, and knockout (KO) mice. These findings underscore the indispensable role of CaMKIIα in associative odorant learning, hinting that reduced CaMKIIα expression may impede effective information transmission between the prefrontal cortex and hippocampus.

171 **Trying, Making Errors, And Revising: A Strategy Of Olfactory Discrimination Learning In Mice**

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In nature, sensory inputs are often noisy and dynamic, affecting perceptual decision-making and reversals. Cognitive flexibility further adds to this complexity. Decision revision allows switching between available choices and/or cessation of already initiated, misconstrued responses. In the present study, we aimed to quantify such behavioral responses and the underlying neural mechanisms. Mice were trained on an olfactory Go/No-Go decision-making task to distinguish between rewarded and unrewarded stimuli. Despite reaching high performance level, they respond inappropriately for a few non-rewarded trials. These trials are defined by a disengaged licking behavior with a higher interlick interval that ceases prematurely within the stimulus window, connoting error awareness. Similar response latency towards the correct responses in an equiprobable Go/No-go

stimuli distribution rules out the component of impulsivity in these trials. Therefore, we interpret this phenomenon as the decision revision. As animals learn, the proportion of engaged commission errors decreases, and revision trials increase, implying an increase in error awareness. Revision trials comprise 5-25% of the high-performance trial blocks. Further, reduced response latency and enhanced performance accuracy in trials following revision, indicate rapid adaptation in their learning strategy. Upon enhancing the inhibitory synaptic signaling in the olfactory bulb by photoactivating ChR2-expressing GABA-ergic granule cells during a complex mixture discrimination task, we observed faster odor discriminations and fewer revision trials, confirming the impact of perceptual load on revisions. In conclusion, we report a learning strategy exhibited by mice to achieve high-performance accuracy during decision-making by response reversals.

173 **Uncovering The Contextual And Behavioral Correlates Of Hdb Cholinergic Activity In Freely Moving Mice**

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Cholinergic neurons of the horizontal limb of the diagonal band of Broca (HDB) modulate olfactory processing through projections to the olfactory bulb (OB) and piriform cortex (PC). While the effects of cholinergic input on odor responses and learning are well-documented, the factors driving HDB neuron activity in awake animals are less understood. To address this, we expressed GCaMP8 in HDB cholinergic neurons in ChAT-cre mice and used microendoscopic calcium imaging to examine their activity under diverse conditions. Building on findings that PC neuron responses to odors shift with experience, we designed a 6-day paradigm to evaluate cholinergic responses in HDB during exposure to novel and familiar environments and odors. Using behavioral tracking with DeepLabCut and SLEAP, we correlated cholinergic activity with behaviors like grooming, sniffing, and proximity to odorants, rather than just odor onset/offset. Interestingly, while novelty usually drives stronger cholinergic responses, we observed robust activity during interactions with bedding—an odor presumed to be familiar. This contrasts with previous findings and suggests that HDB neurons encode familiarity and context more complexly. Preliminary analyses show cholinergic activity correlates with behavior, peaking during investigative bouts and behavioral transitions, regardless of odor novelty. Ongoing work will assess whether HDB responses mirror PC neuron shifts and identify the behavioral factors driving cholinergic activation.

175 **The Impact Of Innocuous Taste Experience On Long-Term Taste Learning And Memory Persistence**

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Both humans and animals learn to reliably avoid or seek foods based on experience. For example, through associative learning, animals learn to avoid tastes that have been previously paired with negative consequences. In a laboratory setting, this is known as conditioned taste aversion (CTA). Recently, we have shown that CTA learning can be enhanced when prefaced with benign taste experiences – a phenomenon we have called Latent Enhancement of CTA learning (LE). For example, taste experience with sour and salty tastes (TE) enhances CTA to novel sucrose 24 hours later (Flores 2016, 2018). Here, we investigate the long term behavioral and neural impacts of LE by testing aversions 24 hours, one week and two weeks post aversion learning in female long evans rats (n=30). We hypothesized that rats who had TE would better retain their aversion at 1 week and 2 weeks post CTA than rats with water experience. Thus far we have replicated the LE phenomenon and demonstrate that animals who received TE, show quicker extinction of CTA learning at the one week test point and stronger retention at the two-week time point. These results suggest different consolidation mechanisms occuring after TE. To better correlate behavior with neural activity, we use immunohistochemistry to tag cells with cFOS and Npas4 (immediate early gene proteins known to be involved in synaptic plasticity and neural activity) in gustatory cortex and the basolateral amygdala after learning. Thus far, the strength of CTA learning correlates with both activity and plasticity measures in both regions. Together these results provide deeper understanding into the LE phenomenon and give insight into how previous taste experiences alter future taste processing and learning.

177 **The Impact Of Taste Hedonics On Latent Enhancement Of Aversion Learning**

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Conditioned taste aversion (CTA) is an intensively studied learning paradigm whereby animals are trained to avoid a taste that has been paired with malaise. Our research has shown that previous benign experience with salty and sour tastes enhances an aversion towards novel sucrose (Flores 2016) -- we have called this phenomenon Latent Enhancement (LE) of aversion learning. LE was associated with enhanced learning-related cFOS expression in gustatory cortex – a region known to process taste learning (GC, Flores 2018). Given that sucrose produces a strong dopaminergic response, it is possible that the LE effect on learning is dependent on the hedonics of sucrose. Here, we hypothesize that LE is not limited to using sucrose as a conditioned stimulus. Long Evans rats (n=9) receive benign experience with sucrose and citric acid prior to learning an aversion towards sodium chloride after which cFOS expression is examined in GC and the nucleus accumbens. After pairing sucrose with an aversion, studies have reported a reduced response in nucleus accumbens signifying a reduction in dopamine. Since our LE paradigm produces a strong aversion, we ask how this activity in nucleus accumbens shifts after taste experience when using different conditioned stimuli (i.e., sucrose versus sodium chloride). We hypothesize that exposure to tastes will reduce dopamine activity in nucleus accumbens post aversion learning when compared to non-experienced aversion controls and that this drop will be greater for sucrose than for sodium chloride. Our data show a replication of the LE effect using sodium chloride as the conditioned stimulus although we did not see an increase in cFOS activity within GC. These results support the LE phenomenon and give insight into the plasticity mechanisms underlying strong aversion learning.

179 **Generalization Of Fear Learning Shaped By Gabaergic Signaling In Early Sensory Processing**

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When a sensory stimulus potentially predicts a threat, that potential shapes the neural representation of that stimulus at the earliest stages of neurosensory processing. This sensory neuroplasticity could play a causal role in the expression of fear or its generalization to new sensory stimuli. In the mouse olfactory system, odor-cued fear conditioning decreases $GABA_B$ receptor expression on the presynaptic terminals of the olfactory nerve, thus increasing the gain of odor-evoked drive into the brain for peripheral neurons excited by the threat-predictive odor. Here we show that this presynaptic change also occurs in neurons that respond to similar odors to which the mouse generalizes its fear, but not in those tuned to dissimilar odors that do not evoke fear. These changes are driven in part by overlap between the sets of neurons representing each odor and in part by spatial proximity of neurons representing the generalization odor to neurons encoding the threat-predictive odor. To test whether these sensory changes are causal, we locally manipulated $GABA_B$ receptor function in the olfactory bulb in mice exploring a scented arena. Control mice that had previously received only ester odor or shock exposures showed no behavioral effect of $GABA_B$ receptor manipulation. However, mice that had previously learned that an ester odor predicted a footshock increased their generalization to also avoid a ketone odor when $GABA_B$ receptors were blocked in the olfactory bulb and decreased their generalization to be less afraid of esters when $GABA_B$ receptors were stimulated in the olfactory bulb. These data demonstrate that fear learning-induced changes in early sensory processing can be instantiated by presynaptic regulation of sensory input and can causally shape behavioral expression of fear generalization.

181 **Investigating The Ligand Selectivity And Tuning Profile Of Homomeric Insect Odorant Receptors**

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Odorant Receptors (ORs) are highly sensitive chemical receptors that respond to a diverse range of volatile compounds. In insects, ORs are ion channels, built from four, seven-transmembrane domain, subunits. In modern insects, all species contain a highly conserved OR co-receptor (ORco), that couples with a highly diversive ORx to create a heteromer. However, in a limited number of basal insects, genome sequencing has revealed an intermediate phase of OR evolution. The Jumping Bristletail (*Machilis hrabei)* was found to have five ORs where none of the ORs resemble a modern ORco. Through previous *in vitro* work, two of the five ORs are robustly expressed in cell culture alone, and display clear signs of activity in the presence of diverse ligands. The structure of one of these ORs, MhOR5, was experimentally elucidated through cryoEM, which opens the door for targeted studies into the mechanisms of ligand binding and receptor activation of insect ORs. In this study, we investigated the broadly tuned MhOR5, and the narrowly tuned MhOR1. We aligned the receptors in both protein sequence and protein structure to determine the residues that form the structure of the canonical binding pocket determined by the cryoEM structure of MhOR5. With this analysis, we perturbed the binding pocket with site-directed mutagenesis to investigate the roles of many of the residues in the binding pocket. These single residue mutants were introduced to structurally diverse ligands to observe how receptor activity is impacted by mutation, and how mutant activity changes by ligand. This work is the starting point for investigating the structural basis of ligand selectivity in insect ORs and will contribute to further work in protein design and engineering in chemoreception.

183 **Computational Models Of The Bitter Taste Receptors Accelerate Modulator Discovery**

John F Trant[1,2,3,4], M. Usman Mirza[1], Michael French[5]
[1]Department of Chemistry & Biochemistry, University of Windsor, Windsor, ON, Canada, [2]Department of Biomedical Sciences, University of Windsor, Windsor, ON, Canada, [3]WE-Spark Health Institute, Windsor, ON, Canada, [4]Binary Star Research Services, LaSalle, ON, Canada, [5]Amaro Therapeutics, New York, NY, United States

The (at least) 26 human bitter taste receptors are not only expressed in the GI tract but are present in tissue throughout the body. The extraoral activity of these GPCRs is not fully understood, and in most cases, human endogenous ligands are not yet identified. Recent progress in the last year, including the release of three independent crystal structures of TAS2R14, highlight the increase in interest in, and the need for better understanding of, these crucial proteins. Over the past three years, the Trant lab in collaboration with Amaro Therapeutics has developed representative computational models of all the proteins in this family. These models are built using tissue-specific lipid membranes and are derived from weighted average models from a wide variety of homology algorithms in the literature as no single algorithm or model was able to generate a useful predictive set of structures. In all cases, *apo*, agonist, and antagonist models have been created and, in some cases, reverse agonist, allosterically inhibited, and partial agonist models have been created. Workflows including ultrahigh throughput AI-assisted screening of libraries (1.3 trillion compounds), rigid docking, induced-fit docking, molecular dynamics simulations, free energy perturbation, and single point quantum mechanical calculations have been used to better understand the likely binding modes of both known ligands, and predict the identity of both new active compounds and to suggest likely ligands for orphan receptors. The presentation will discuss the creation of the model, the validation and use of the model for therapeutic and taste masking purposes, and a case study of the binding preferences of TAS2R14— and an examination of KDT-501, a known agonist of TAS2R1.

185 **Identification Of Novel Tas2R4 Agonists By Screening Of A Natural Compound Library**

Sara Montelatici[1], Bernd Bufe[2], Marcel Winnig[1]
[1]Axxam SpA, Milan, Italy, [2]Kaiserslautern University of Applied Sciences, Zweibrücken, Germany

The NatPure compound library, one of the largest collections of pure natural compounds, comprises around 15,000 molecules from diverse plant and microbial origins. It's chemical diversity and with about 30% of its compounds being novel and unpublished, it serves as a unique resource for drug discovery and taste research. We performed a screening campaign to identify novel TAS2R4 ligands and identified new compounds from different classes activating TAS2R4. Interestingly, some of the newly identified compounds do not contribute to bitterness perception. This result supports a broader role for TAS2R4 signaling, and may suggest physiological effects in disparate organs in which the receptor is expressed. This opens new research avenues for understanding the broader physiological roles of taste receptors and the therapeutic potential of these non-bitter agonists in both pharmaceutical applications and in the food industry.

187 **Molecular Basis For Activation Of The Human Bitter Taste Receptor Tas2R14 By Ritonavir**

Jiao Wen, Xinyi Ma, Xinyi Zhou, Yongcheng Lu, Yukyoung Kim, Young Seo Lee, Alice Lee, Shurui Chen, Keman Xu, Meng Cui
Northeastern University, Boston, MA, United States

Ritonavir is a protease inhibitor used in combination with other antiretroviral medications to treat HIV, particularly in children. It increases the bioavailability of these medications by inhibiting the cytochrome P450-3A4 enzyme and is also being studied for cancer treatment due to its mechanism of action. However, its intense bitterness, especially in liquid formulations, may be intolerable for some children. This bitterness is attributed to its activation of bitter taste receptors, including TAS2R14, as demonstrated in our previous study. In this study, we utilized molecular modeling, site-directed mutagenesis, and cell-based calcium mobilization assays to characterize the key residues involved in TAS2R14 activation by ritonavir. These results are crucial for the design and screening of bitter taste inhibitors.

6:00 - 7:00 PM	Calusa Foyer
Networking Reception	

7:00 - 8:20 PM	Calusa EFGH
Polak Awards Lectures	

The Polak Foundation Awards are awarded in honor of the Elsje-Werner-Polak Memorial Fund in memory of our niece gassed by the Nazis in 1944 at age 7: Ghislaine Polak and the late Ernest Polak.

Chair(s): Ann-Marie Torregrossa

The Molecular And Cellular Mechanisms Of Alkaline Taste Sensation In *Drosophila*

Tingwei Mi[1], John Mack[1], Wyatt Koolmees[1], Quinn Lyon[1], Luke Yochimowitz[1], Zhao-Qian Teng[2], Peihua Jiang[1], Craig Montell[3], Yali Zhang[1,4]

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Animals, including insects and humans, rely on their sense of taste to identify nutritionally beneficial foods and avoid harmful substances, a critical function for survival. While acid-sensing mechanisms are well-characterized, the detection processes for alkaline foods remained poorly understood. Here, we investigate the molecular and cellular mechanisms underlying alkaline pH detection using the fruit fly *Drosophila melanogaster* as a model organism. We identify Alka, a pentameric chloride channel activated by hydroxide ions (OH^-), as a key player in this process. Alka is specifically expressed in the labellum's gustatory receptor neurons (GRNs). Behavioral assays reveal that wild-type flies exhibit an innate aversion to alkaline foods, while alka mutants show significant deficits in this behavior. Structural studies using cryo-electron microscopy and functional analyses through patch-clamp recordings confirm Alka's ion channel properties. Furthermore, optogenetic activation of Alka-expressing GRNs induces aversive responses to sucrose, whereas silencing these neurons impairs aversion to high-pH foods. These findings establish Alka as a novel taste receptor for alkaline foods, providing critical insights into the mechanisms of alkaline pH detection in animals. This work expands our understanding of taste receptor functions and sets the stage for exploring alkaline taste perception in other organisms.

Identification Of Putative Oral Mechanosensory End-Organs

Debarghya Dutta Banik[1], Tao Tang[1], Nicholas P. Weber[2], Suzanne I. Sollars[2], Brian A. Pierchala[1]

[1]Department of Anatomy, Cell Biology & Physiology, Stark Neurosciences Research Institute, Indiana University School of Medicine, Indianapolis, IN, United States, [2]Department of Psychology, University of Nebraska at Omaha, Omaha, NE, United States

Oral mechanosensation is critical in feeding behaviors, grooming, and speech. The mechanosensory neurons innervating the tongue and oral cavity convey the textural properties of the food, such as crispiness, creaminess, and graininess, to the central nervous system. This bestows appetitive or aversive characteristics, resulting in food being consumed or rejected. Recent studies have identified RET+ neurons in both Geniculate and Trigeminal ganglia that are indispensable for oral mechanosensation. RET is the signal-transducing receptor for the Glial Cell Line-Derived Neurotrophic Factor (GDNF) Family Ligands (GFLs). These four GFLs (GDNF, Artemin, Neurturin, Persephin) bind to co-receptors comprised of one of the GFRas (GFRa1-4), which then bind and activate RET. In this study, we characterized the expression of GFLs in the lingual epithelium using recently developed reporter lines and found GDNF and Artemin expression in the lingual epithelium in and around Fungiform taste papillae. Using intersectional genetics, nerve transection, and immunolabelling, we discovered that RET and GFRa1 dual positive fibers originating from Geniculate ganglia make contact with both GDNF+ and Artemin+ cells in the lingual epithelium. Finally, using FM 1-43 dye labeling, we identified that food-activated Piezo2+ mechanosensory fibers in the tongue represent a spatial map of mechanosensory fiber activation depending on food textures. Stiffer textures mainly activate fibers on the upper part of the taste buds, while softer textures selectively activate fibers below or at the base of the taste buds. Our data indicate that the GDNF+ and Artemin+ cells on the lingual epithelium might act as putative oral mechanosensory end organs, with GFRa+ and GFRa3+ fibers acting as the principal mechanosensory terminals.

Olfactory Bulb Activity And Active Sniffing During Naturalistic Foraging In Freely Moving Mice

Jesse A. Smith[1], Kevin Bolding[2], Jiayue Tai[3], Ian Davison[1]

[1]Boston University, Boston, MA, United States, [2]Monell Chemical Senses center, Philadelphia, PA, United States, [3]Tufts University, Medford, MA, United States

Understanding the critical role of the olfactory system in guiding naturalistic foraging behaviors promises to

provide fundamental insights into sensory perception and ecological adaptations. Mice rely heavily on their olfactory senses to navigate complex environments and locate potential food sources. Although odor-evoked activity has been intensively studied in head-fixed animals, little is known about the dynamic sensory signals acquired by freely moving animals when actively sampling their environment. To address the gap in knowledge about real-time olfactory sensory-motor strategies, we engineered a novel large-area miniscope allowing us to image glomerular activity across both hemispheres of the main olfactory bulb (MOB). MOB imaging in freely moving animals revealed that sensory information was largely confined to distances within 10 cm of the odor source. Average glomerular activation increased with proximity to odor sources, allowing us to map well-studied concentration-dependent coding onto spatial measures. Interestingly, glomerular activity often showed directional tuning near the odor source, and these signals predicted future turning behavior. We used implanted thermistors to directly relate sniffing activity to behavior and neural activity, revealing that animals only obtain sensory information on a relatively sparse subset of sniff samples. Integrating sniff and imaging measurements should help reveal how active sampling strategies inform moment-to-moment navigational decisions during odor source localization.

Reevaluating Odor Mixtures: Evidence For Predominant Linearity

Robert Pellegrino[1], Jennifer Margolis[1], Carissa Evans[1], Mathew Andres[1], Emily Mayhew[2], Alex Wiltschko[3], Rick Gerkin[3], Joel Mainland[1,4]

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Recent models have shown that physicochemical properties of individual molecules can be used to accurately predict perception. But predicting the perception of natural odors, which often consist of complex mixtures of chemicals, remains elusive. It has been reported that odor quality can shift dramatically depending on the specific combination of odorants, even when individual components remain constant, with one example being configural perception, where the combination of odorants gives rise to a new, emergent perceptual quality distinct from the qualities of the individual components. However, linear models, which assume no emergent effects, have performed well at predicting odor mixture similarity in human behavioral studies, raising the question of how often odor mixtures exhibit linear behavior. To test this, we collected descriptive ratings for a large, diverse set of mixtures (N = 706) and their components (N = 524). Only one out of 706 mixtures (<0.14%) had a quality that could not be explained by a linear combination of the qualities of the components. To further challenge the linear model, we collected descriptive ratings for eight previously reported mixtures showing configural processing and their component odorants (e.g., caramel + strawberry = pineapple). These mixtures showed linear behavior and a linear model predicted odor perception with high accuracy (r = 0.82). We conclude that most odor mixtures fall within a region defined by linear mixing of their components, challenging prior assumptions in the field. This has broad implications for industries such as flavor and fragrance, as well as environmental monitoring and health, and suggests that good mixture perception models are possible without building in configural assumptions.

Friday, April 25, 2025

7:30 - 9:00 AM	Estero Foyer
Continental Breakfast	

8:00 - 10:00 AM	Estero Ballroom
Poster Session III	

200 **A Natural Lesion Model Unravels The Nature Of Chemical Fear Communication**

Jasper H.B. de Groot
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Debunking the human tiny smeller myth, scientific research has revealed that humans have excellent smell abilities, including social communication. Studies show that humans convey adaptive social information, such as emotions, through body odor, synchronizing senders and receivers via behavioral, affective, and neural responses. However, the question of whether humans use pheromones—species-wide chemical signals that trigger innate responses—for social communication remains unresolved, presenting a multidisciplinary challenge beyond the scope of psychology. To investigate this, we combined insights from chemical analyses of fear odors with a study of patients with Urbach-Wiethe Disease (UWD), an extremely rare, recessive genetic condition marked by basolateral amygdala (BLA) calcification, while other brain regions remain intact. Notably, BLA damage causes hyper-responsiveness to unconditioned fear stimuli and impaired fear learning, making UWD a unique natural lesion model to examine whether human chemical communication relies more on innate or learned mechanisms. In South Africa, where UWD is more prevalent, we established a custom-built lab space with an airport-transportable olfactometer. A double-blind within-subjects experiment was conducted with 5 UWD patients and 14 controls matched on age, gender, IQ, and smell ability. Participants smelled three odors—fear (synthesized molecules from chemical analysis), disgust (isovaleric acid, resembling sweat), and neutral (odorless air)—while classifying morphed faces (35% to 65% fear-disgust continuum). Results revealed a significant and strong hyperfear-perception bias in UWD patients (Cohen's $d = 1.15$), highlighting that fear odor could be synthesized and that the BLA has a critical role in potentially innate human chemical communication.

202 **Child Food Neophobia And Sympathetic Arousal In Response To Odor Exposure**

Agnieszka Sorokowska[1], Anna Oleszkiewicz[1,2], Sabina Barszcz[1], Dominika Chabin[1], Aleksandra Kamieńska[1], Piotr Jędrusik[1], Łukasz Kaczmarek[3], Piotr Sorokowski[1], Thomas Hummel[2]
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Child food neophobia (CFN) refers to the rejection or avoidance of novel foods in childhood. In our recent psychophysical study, we observed that higher CFN was linked to poorer olfactory abilities. Paradoxically, children with CFN are often described as being highly sensitive to sensory qualities, including the olfactory aspects of food. Here, we examined an arousal-based mechanism that might explain this inconsistency. Hypothetically, odors – particularly those that are unfamiliar or food-related – may generate heightened (unpleasant) sympathetic arousal in (sensitive) children with CFN. This heightened arousal could reduce their olfactory exploratory behaviors and hinder olfactory development, resulting in poorer performance on smell tests. We investigated this hypothesis by measuring sympathetic arousal in response to six food and non-food odors varying in familiarity in 95 children (46 girls) aged 4–9 years. Data were collected using a BioPac MP36 physiological amplifier and analyzed via AcqKnowledge software (BioPac Systems, USA). Using linear mixed models, we assessed the response amplitude of electrodermal activity as an index of sympathetic arousal following odor exposure relative to characteristics of children (CFN, anxiety, odor identification scores, age, gender), caregivers (food neophobia, age), and odors (pleasantness and familiarity ratings, edibility and presentation order). Regarding the main study hypothesis, results indicated that self-assessed CFN was not significantly related to response amplitude. At the same time, response amplitude was positively predicted by the child's odor identification score. These findings suggest that heightened sympathetic arousal in response to odors may not be the mechanism explaining the previously observed inconsistencies in the literature.

204 **Chemosensory Detection Of Predator-Derived Kairomones And Associated Behavior In Mice**

Jinxin Wang, Varun Varun, Julian Meeks
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Mammalian social interaction relies heavily on chemosensory information processed by olfactory pathways. In terrestrial mammals, the accessory olfactory system (AOS) is specialized for detecting non-volatile cues,

including kairomones (interspecific social cues) and pheromones (conspecific social cues). Our understanding of most natural AOS ligands, their receptors, and the behaviors they govern is still limited. Here, we present research on the chemosensory mechanisms involved in detecting and responding to predator snake feces-derived kairomones. Aqueous extracts of Eastern Massasauga Rattlesnake selectively activated a subset of vomeronasal sensory neurons (VSNs) in an *ex vivo* Ca^{2+} imaging assay. To identify molecules in snake feces that serve as VSN ligands, we fractionated snake feces extracts using reverse-phase high-performance liquid chromatography (RP-HPLC) and identified several fractions that retained the capacity to activate VSNs. Subsequent liquid chromatography-mass spectrometry (LC-MS) analysis of these subfractions identified several candidate molecules enriched in snake feces, including bile acids, metabolites, and fatty acids. To investigate the behavioral effects of mouse predator cues, we employed a machine learning (ML)-based analytical workflow to measure behavior from high-resolution 2D/3D videos precisely. The results indicate that mice display distinct behavioral patterns to snake feces compared to feces from non-mouse-predators. Taken together, these results suggest that a novel population of VSNs detects reptilian mouse predator chemosignals, and that their activation elicits distinct threat assessment responses. This research will provide the basis for identifying kairomone ligands and corresponding receptors that drive behavioral responses to environmental threats.

206 **Cooking Odors, But Not Food Consumption, Influence Body Odors And Social Judgments**

Jessica Gaby[1], Pete Hatemi[2], Helene Hopfer[2]

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Olfactory cues facilitate differentiation of ingroup and outgroup members across animal species. Human body odor may be affected by culturally-influenced personal care or dietary choices. Do humans utilize these odor cues to determine group identity? Some cultural stereotypes claim that members of ethnic/racial groups smell like certain foods. Does diet contribute metabolic or environmental group membership cues? We compared the influence of eating curry to added curry cooking odor on hedonic and social judments of body odor. Our “eater” group (n=8) ate 10g of Indian-style curry for 28 days; our “smeller” group (n=6) smelled curry paste but did not eat it. We collected shirts on days 0 and 28; we added a cotton ball infused with curry cooking odor to half of the smellers’ shirts. Shirts were judged by “ingroup” raters (i.e., eaters smelled shirts of other eaters) and by naïve “outgroup” raters (n=17 for eaters, 19 for smellers). Eating curry did not impact hedonic or social ratings of body odors except for perceived intensity by outgroup raters $F(1, 247) = 4.5$, $p = .035$. Added cooking odor resulted in lower pleasantness ratings by ingroup ($F(1, 71) = 8.65$, $p = .004$) and outgroup raters ($F(1, 246) = 12.66$, $p < .001$), and a lower number of body odors categorized as American (ingroup $p = .035$, outgroup $p < .001$) and Caucasian (ingroup $p = .001$, outgroup $p = .003$). Interestingly, ingroup raters perceived shirts with added cooking odor as more familiar ($F(1, 71) = 20.64$, $p < .001$), suggesting that food odors may indeed facilitate identification of ingroup members. The results of this work suggest that food-related stereotypes are likely driven by cooking odors rather than metabolic byproducts of diet, and highlight the potential for exposure to unfamilar foods to decrease outgroup prejudice.

208 **The Impact Of Smelling Hexadecanal On Startle Response In Men And Women**

Juna Khatib, Tali Weiss, Ofer Perl, Noam Sobel
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Hexadecanal (HEX) has been identified as a possible social chemosignal in rodents where it may contribute to social buffering (Klein et al, 2015). Moreover, given conservation of its cognate OR37B receptor, Hoppe et al (2006) suggested HEX may act across species. Consistent with this, in Mishor et al (2021) we found that exposure to HEX reduces reactive aggression in men but increases it in women, and in Endevelt-Shapira et al (2018) we found that it reduces startle response in men. Given the potential clinical value of a smell that can reduce anxiety, we test the hypothesis that HEX will have a sex-specific impact on startle response. In a within-subjects experiment, participants experience 20 startle events (50 ms□95 dB) at semi-random inter-stimulus intervals of 30-90 seconds under three separate conditions across three days: HEX obscured in lavender, lavender alone, no odor. We measure electrocardiogram, galvanic skin response, respiration, and eyeblink electromyography to estimate the startle response. A concern in this design is possible cross-day habituation in startle. To test for this we ran 5 participants in the full 3-day pilot study. We observed evidence for a decline in startle within the session (Session 1: $r = -0.562$, $p = 0.011$; Session 2: $r = -0.141$, $p = 0.551$; Session 3: $r = -0.510$, $p = 0.023$), but importantly, not across sessions (repeated measures ANOVA: $F(2,8) = 0.526$, $p = 0.610$). This validates the design where we will now study 30 men and 30 women under the three intended conditions, in order to estimate the effects of HEX on startle.

210 **Expression Of Familial Dysautonomia-Causing Gene *Elp1* In The Peripheral Taste System Is Important For The Development Of Taste Papillae And Buds**

Md Mamunur Rashid[1], Wenxin Yu[1], Ruchi Sha[1], Zhonghou Wang[1], Frances Lefcort[2], Hong-Xiang Liu[1]

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Elongator complex protein 1 (*Elp1*) is important for neurogenesis and neuronal survival. The essential roles of *Elp1* in the development and maintenance of taste organs is implicated by the loss of taste papillae and buds in patients with Familial Dysautonomia (FD) caused by *Elp1* mutation. To understand the potential stage-specific roles of *Elp1* and tissue involvement in taste papilla and bud formation and maintenance, we examined *Elp1* expression patterns in the tongue and cranial ganglia at various developmental stages using *Elp1-LacZ* transgenic mice and analyzed the phenotypes in *Elp1* conditional knockout (*Elp1 cKO*) driven by *Sox10-Cre* that labels

neural crest lineages. Our findings revealed a dynamic *Elp1* expression in tissue compartments associated with taste papilla and bud development. In the tongue epithelium *Elp1* was broadly expressed at E12.5 and restricted to the basal epithelial cells at E14.5, P1 and adult. *Elp1* was also observed in taste buds in adult mice. In the tongue mesenchyme, *Elp1* was widely expressed at the examined stages mentioned above. In geniculate and trigeminal ganglia, *Elp1* was expressed in nearly all neurons at embryonic and postnatal stages. *Elp1 cKO* mice depicted impaired taste organogenesis, including fewer papillae on the slightly smaller tongues at E13.5, fewer and less profound fungiform papillae and smaller circumvallate papilla at E19, fewer and smaller circumvallate taste buds in a rarely survived postnatal mouse at day 13. Our data reveals *Elp1* expression in multiple associated tissue compartments of the developing tongue, and important role of *Elp1* in the neural crest lineage for taste organogenesis. Studies using tissue- and stage-specific *Elp1 cKO* will be needed to define the roles of *Elp1* in the development and maintenance of taste papillae and buds.

212 **Glp-1 Receptor Agonists Significantly Impair Taste Function**

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

214 **Sars-Cov-2 Infection Of Taste Bud Cells In Human Ace2 Transgenic Mice**

Kang-Hoon Kim[1], Emma Larsson[1], Heaven Branch[1], Richard Bowen[2], Hong Wang[1]
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Taste loss is particularly prevalent with SARS-CoV-2 infection. In the early phase of the COVID-19 pandemic, close to half of patients reported taste loss. While taste function was restored quickly in many patients, a subset of patients suffered from sustained taste loss that lasted longer than several months. How SARS-CoV-2 infection leads to taste dysfunction remains poorly understood. To study the underlying mechanism of taste loss, we used transgenic mouse models that express the human angiotensin-converting enzyme 2 (ACE2), the receptor for SARS-CoV-2 in humans. We used the human ACE2 (hACE2) knock-in and mouse ACE2 knockout strain that has been shown to be susceptible to SARS-CoV-2 infection. Our results show that taste tissues can be infected by SARS-CoV-2, both viral RNAs and proteins can be detected. Antibody staining experiments show that SARS-CoV-2 can infect types II and III taste bud cells that are responsible for sensing sweet, umami, bitter, and sour tastes. In addition, we generated mouse strains that express hACE2 but lack the antiviral gene, interferon regulatory factor 3 (IRF3) or type I interferon receptor 1 (IFNAR1). Recent studies showed that inborn genetic errors in key antiviral genes exist in human populations and are highly enriched in patients with severe COVID-19. Thus, the double-transgenic mouse strains allow us to investigate whether deficiencies in antiviral genes contribute to SARS-CoV-2-induced taste loss. We found that taste tissues of IRF3-knockout mice contained detectable SARS-CoV-2 RNAs at 36 days post infection, while viral RNAs were cleared from taste tissues of mice with functional IRF3. Our results suggest that deficiency in IRF3 leads to prolonged viral infection in taste tissues, which may contribute to long-term post-viral taste loss.

216 **Bitter Maternal Diet Increases Offspring Bitter Acceptance In 24-Hr Feeding Trials But Not Brief-Access Taste Tests**

Verenice Ascencio Gutierrez[1], Samantha L Brooker[1], Kamila D Nixon[1], Emily Demieri[1], Jyothi Vasavan[1], Ann-Marie Torregrossa[1,2]
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It has been well documented that offspring show increased acceptance for flavors consumed by the mother via indirect exposure through the amniotic fluid and/or maternal milk. Our lab has recently shown that in adult rats, repeated exposure to a diet alters the salivary proteins (SPs), which, in turn, alters the acceptance of the bitter diet. However, it is unclear if repeated exposure via the maternal diet (MD) alters the salivary proteome and diet acceptance of offspring. To test this, we gave female rats a 0.375% quinine maternal diet (Q-MD) or an equicaloric control diet (C-MD) from pre-breeding through lactation. Dams and offspring were housed in custom cages that limit offspring exposure to experimental diets by elevating the food cup. All pups were given the control diet at weaning on postnatal day (PD) 21. Q-MD offspring were smaller than C-MD offspring ($p<0.05$). Q-MD offspring showed higher expression of SPs we associate with quinine eating (23 and 37 kDa bands, p's <0.05). A subset of the animals were fed the quinine diet between PD 35 and PD 40 during a two-day feeding

trial. Offspring from quinine fed mothers ate more of the diet on the second day than those of control fed mothers ($p = 0.05$). A second group of animals was offered varying concentrations of quinine and sucrose in brief-access taste tests. C-MD and Q-MD offspring did not differ in taste-guided responding to quinine or sucrose ($p's > 0.05$). These data suggest that maternal diet alters the rate of diet acceptance and demonstrates maternal diet has the capacity to alter the salivary proteome.

218 **Role Of The Aryl Hydrocarbon Receptor In Taste Cells**

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The aryl hydrocarbon receptor (AHR) is a ligand-activated transcription factor that is activated by dietary small molecules, microbial metabolites and pollutants. AHR is known to have varied roles in the regulation of epithelial regeneration, xenobiotic and drug detoxification, and host-microbiome interactions. In this study, we aimed to investigate the roles of AHR in taste cells using scRNASeq, RNAscope, immunohistochemistry, qPCR and brief access taste tests in C57BL/6J (WT), *Ahr* hypomorphic ($Ahr^{fx/fx}$), and *Ahr* conditional knockout ($Ahr^{\Delta Krt5}$) mice. scRNASeq and histological analyses revealed *Ahr* expression in taste cells and duct cells of Von Ebner's gland addition along with multiple subtypes of lingual immune cells including T and B cells, all three subtypes of innate lymphoid cells, monocytes, macrophages, Langerhans cells, neutrophils, and mast cells. RNAscope analysis showed widespread expression of the *Ahr* in the taste papillae and associated von Ebner's glands. $Ahr^{\Delta Krt5}$ mice showed an altered preference for a subset of sweet and bitter taste stimuli. Finally, we determined the changes in gene expression in $Ahr^{fx/fx}$ and $Ahr^{\Delta Krt5}$ mice using bulk RNASeq. Our results show that *Ahr* is involved in taste signalling and might regulate taste gene expression and taste cell regeneration. In addition, we believe that *Ahr* may regulate taste-oral microbiome interaction and immunity. Our study lays the groundwork for future studies on the role of this fascinating transcription factor in taste papillae.

220 **Consumer-Affordable Practices For Reducing Sodium Intake: Insights From The Sal&Mieux Project On Discretionary Salt**

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Excessive salt consumption is a public health concern, yet reducing salt in food is often associated with diminished taste. Discretionary salt (DS), directly added by consumers, significantly contributes to overall sodium intake but remains underexplored. The French research project Sal&Mieux aimed to identify strategies for reducing salt intake by examining domestic cooking and seasoning practices that optimize DS use. We specifically assessed three actionable factors in domestic seasoning: the timing of DS addition, the shape and size of DS crystals, and flavorings addition. Sensory evaluations with consumer panels rated saltiness, flavor attributes, adequacy of salty taste using Just-About-Right (JAR) scales, and liking for three common foods: carrots, chicken, and pasta prepared using standard recipes. Sodium magnetic resonance imaging (^{23}Na MRI) experiments mapped salt distribution in food under different salting conditions. The results showed that adding salt after cooking significantly increased salty taste intensity across all foods, with fleur de sel having the strongest effect. MRI findings confirmed that, under these conditions, salt remains on the food surface, enhancing its availability to taste receptors. Additionally, smoked garlic and smoked bacon flavorings significantly enhanced saltiness perception through Odor-Induced Saltiness Enhancement (OISE). JAR and liking data further demonstrated that sprinkling fleur de sel post-cooking, potentially combined with specific sodium-free flavorings, helps reduce DS use while maintaining taste and acceptability. These findings offer practical strategies to optimize domestic salting practices and reduce sodium intake without compromising food liking. This work was supported by the Agence Nationale de la Recherche (ANR-19-CE21-0009 Sal&Mieux).

222 **Behavioral Effects Of Chemogenetically Silencing Mouse Peripheral Taste Processing**

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Chemogenetic silencing uses inhibitory Designer Receptor Exclusively Activated by Designer Drugs (DREADD) to target neurons within a pathway. While many central sensory pathways have been explored using this tool, it has not been applied to peripheral taste processing. Initially, we validated the approach by expressing inhibitory DREADD in all peripheral sensory neurons (*Pirt*;hM4Di). After confirming expression, we injected a DREADD agonist, clozapine-N-oxide (CNO), intraperitoneally at 0.1-5mg/kg into *Pirt*;hM4Di mice. As expected, inhibition of proprioceptors severely reduced muscle tone and blocked motor function, confirming silencing. Next, we tested a transcriptionally and functionally distinct subset of gustatory neurons which express proenkephalin (Penk) and respond to sour, bitter, and high-salt stimuli. We measured lick rates of water-deprived *Penk*;hM4Di mice to preferred (water, 100mM sucrose) and avoided solutions (20mM citric acid [CA], 0.1mM quinine [Q], 890mM NaCl) following injection of either saline or 0.5-5mg/kg CNO. As expected, CA, Q and NaCl were strongly avoided in the control but also in the presence of CNO. Further, *Penk*;hM4Di mice increased overall drinking with CNO. To assess the basis for this increased consumption, we recorded *ad lib* water drinking of *Penk*;hM4Di mice to analyze licking microstructure. Compared to saline, CNO significantly increased water

consumption, total licks, and burst duration and size; these effects were not observed in control mice. Possibly, in *Penk*;hM4Di mice, CNO acts on neurons in the hypothalamus to increase thirst or mechanosensors in the stomach to decrease feedback, thereby masking gustatory inhibition. We are continuing these studies with other strains of mice to assess the behavioral effect of chemogenetically silencing gustatory neurons.

224 **Neophobia To Saccharine Attenuated By Only Brief Exposure**

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Animals must simultaneously explore novel stimuli and avoid being harmed by them. In the context of feeding, achieving this balance involves a phenomenon known as attenuation of neophobia (AN): novel foods—even delicious ones—are consumed in a limited amount at first; only after some experience do animals increase their consumption (Lin et al., 2012; Miller & Holzman, 1981). While this learning phenomenon is typically studied across days, more rapid changes in consumption (or more accurately of hesitancy in consumption) have been found to occur even within the first tasting session (Monk et al., 2014) using brief access to trials of saccharine (0.028M). Here, we used this brief-access task (BAT) to explore this fast AN, asking whether it depends on time or amount of exposure. After reproducing Monk et al., we hypothesized that AN is dependent on receiving a consistent series of taste exposures and that small amounts of taste exposure would not fully attenuate neophobia. To test this hypothesis, we limited a group of rats to only 10 seconds of 0.028M saccharine access in a one-bottle BAT trial and measured their consumption on 4 subsequent days during full 15-minute trials. Surprisingly, their consumption, number of licks, and lick rate on the second day were not statistically different from a control group that received all 15 minutes of exposure on the first day instead. Furthermore, on the first exposure of the first day, all groups robustly show a characteristic short bout that is not present on subsequent days. These results demonstrate that even 10 seconds of exposure (~50 licks, ~0.2 grams) can fully attenuate neophobia. These data cast AN as an all-or-none effect that can be elicited by very small amounts of taste exposure.

226 **Mechanism Of Sweet Taste Plasticity In Response To A High-Sugar Diet**

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A chronic high-sugar diet reduces sweet neural responses, but the underlying mechanisms remain poorly understood. We investigated Activity-Regulated Cytoskeleton-associated protein (Arc1), a regulator of neural plasticity known for its roles in synaptic protein localization, transcription regulation, and intercellular signaling using *Drosophila melanogaster*. Translating Ribosome Affinity Purification (TRAP) sequencing data revealed reduced *Arc1* RNA expression in sweet neurons under a high-sugar diet. Immunostaining showed Arc1 expression predominantly around cell bodies of sweet neurons in the labellum, suggesting its presence in sweet neurons and nearby thecogen cells, which are support cells enveloping taste neurons. Functional studies with electrophysiology and behavior assays demonstrated that Arc1 mutants exhibit diminished sweet responses, highlighting Arc1's role in sweet taste sensation and plasticity. These findings provide new insights into molecular mechanisms driving taste modulation in response to dietary changes.

228 **The Role Of Stimulus Temperature On Salt Perception And Central Gustatory Representation In Behaving Mice**

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The experience of consuming food and beverages results in multimodal sensations that involve the integration of intraoral gustatory, retronasal olfactory, and somatosensory cues that all contribute to the percept of flavor. Human psychophysical studies that have focused on just the gustatory and somatosensory cues have shown, although equivocal, that temperature can influence taste perception and contribute to food and beverage preferences that influence how much we eat. For example, if temperature alters the perceived intensity of table salt (NaCl), this could result in a diet high in sodium which can cause serious health consequences such as high blood pressure, stroke, and other cardiovascular issues that can increase the risk of, or even cause, death. Therefore, it is crucial to investigate how temperature modulates salt sensitivity and influences the central salt representation in behaving mice. Here, we used a behavioral two-response taste detection task, brief access preference test, and electrophysiological recordings from electrodes and silicon probes to investigate how temperature modifies the sensory-discriminative and hedonic properties of sodium (NaCl) and non-sodium (KCl) salt taste. We found that 1) the mice had higher detection thresholds when both salt solutions were presented at 14°C compared to when they were presented at 36°C, 2) mice had an amiloride-dependent increase in preference for 0.6M NaCl when presented at 36°C and 3) temperature strongly impacts NaCl and KCl concentration coding in the gustatory cortex (GC). These results obtained in mildly water deprived mice, imply that temperature massively shapes the salt responses of GC neurons, and that colder salty foods and beverages might be harder to detect compared to warmer salty foods and beverages.

230 **Accuracy And Temporal Precision Of Open-Source Machine Learning Models For Lick Detection**

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Lickometers using photobeams or capacitance circuits have been developed for the analysis of consummatory behaviors. While these techniques can detect licks with high accuracy and temporal precision, they lack the ability to track other orofacial behaviors which provide valuable insight into taste responses. We focused on the precision and accuracy of lick detection through video analysis from supervised machine learning models trained via open-source software. We used DeepLabCut (DLC), a pose-estimation software that is supported by Simple Behavioral Analysis (SimBA), to classify orofacial behaviors using metrics derived from pose information. Head-fixed, water restricted C57Bl/6 mice were placed on a treadmill and trained to lick a spout after a brief tone. Videos of the ventral aspect of the face were acquired either at 30, 60, or 160 fps; respiration was detected with an external thermistor wire placed in front of one nostril. Lick detection accuracy was determined by comparing the output of a capacitance circuit lickometer to DLC pose estimation of tongue location and a region of interest (spout), and a behavior classification model trained in SimBA on spout licks. Temporal precision was determined through the lens of respiratory phase preference of licks using thermistor data collected at 25k Hz and down-sampled to 2000 Hz. Analyses were performed on videos at each frame rate. While the accuracy of lick counts appears unaffected by frame rate, temporal precision of lick detection decreases as frame rate decreases. Behavioral analysis performed on videos acquired at 160 fps yields a similar respiratory phase preference, suggesting its temporal resolution is sufficient for detailed analysis of electrical signal acquired at 25k Hz.

232 **Fatty Acid Preference Differs Between Ob/Ob And Wt Mice**

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The leptin deficient (*ob*/*ob*) mouse model develops obesity at a high rate, in part due to the inability to regulate satiety after feeding. Leptin also regulates endocannabinoids levels in the hypothalamus, and in the case of the *ob*/*ob* model, leptin deficiency means high endocannabinoid tone and reinforcement of feeding behaviors. Obesity and high endocannabinoid levels have been correlated with taste insensitivity in rodents and humans, leading to greater consumption of calorically dense foods. Whether fatty acids are included in this general taste insensitivity is not well understood. Our objective was to determine if *ob*/*ob* mice display a higher preference for individual fatty acids over Wild-type (WT) mice. 24 mice (12 WT and 12 *ob*/*ob*) were given a two-bottle preference test to determine percent preference. Mice were tested in groups of 3 and water fasted for 21 hours prior to the start of the test. The test solution contained oleic acid as a sodium salt (NaOleate), which allows for the simple dissolving in water. NaOleate was tested at 4 different concentrations, 0.5mM, 1.58mM, 5mM and 15.8mM. Our results showed that all groups significantly preferred the 1.58mM concentrations of NaOleate over water but *ob*/*ob* mice significantly preferred the 0.5mM and 5mM concentrations over water as well ($p<0.05$). No preference was shown for the 15.8mM concentration. These results suggest that rodents can detect individual fatty acids, such as oleic acid, in solution and prefer to drink these solutions over those not containing the fatty acid. Mice with leptin deficiency and obesity seem to have an even higher preference for these fatty acid solutions than WT mice. This has important implications for the overconsumption of highly palatable, fatty foods in our society.

234 **The Role Of Trpm8 Thermoreceptors And Temperature In Sweet Taste Preferences In Mice**

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The role of transient receptor potential melastatin 8 (TRPM8) thermoreceptors in oral sensory preferences in rodents is beginning to be explored. Previous work from our lab has shown that TRPM8 contributes to warmth perception and loss leads to a “blurring” effect between cool and warm temperatures. It is unknown how TRPM8 signals contribute to taste preferences. Here, we studied the role of TRPM8 on sweet taste preferences in a thermal brief-access fluid licking assay. To test this, an initial squad of C57BL/6J (B6; $n = 6$) and TRPM8 gene deficient (M8 -/-; $n = 6$) mice were proffered temperature-controlled sucrose solutions in a custom thermo-lickometer at either low (0.1 M) or elevated (0.5 M) concentrations in combination with being precisely warmed (30°C) or cooled (15°). Six temperature-concentration pairings were counter-balanced across subjects and experimenters were blind to genotype. A second squad of mice (B6; $n = 6$, M8 -/-; $n = 6$) were proffered glucose under the same methodological conditions. Results show B6 mice preferred 0.5 M of either sweet stimulus at 30°C compared to 0.1M concentration at 15°C whereas the M8 -/- mice appeared indifferent (ANOVA, $p < 0.5$). Secondly, B6 mice preferred 0.5 M sucrose over 0.1 M when both were 30°C. However, M8 -/- mice were indifferent to 0.1 M sucrose and 0.5 M at 30°C (ANOVA, $p < 0.5$). This suggests that M8 -/- mice less prefer tastes at 30°C and may be “blurring” this temperature with warmer, more aversive temperatures, as suggested by a model in our prior study. These data, suggest that sweet taste preferences are influenced by temperature and highlights the role of TRPM8 in warm thermosensation. This experiment is ongoing, and further testing will be performed to increase the sample size.

236 **The Role Of Trpm8 Function In Thermosensory Effects On Glucose Taste Preferences In Mice**

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Oral thermosensation shapes perceptual and neural responses to tastes that are intricately linked to ingestive behavior and various human disorders. The transient receptor potential melastatin 8 (TRPM8) ion channel, a cold receptor on trigeminal fibers, plays a key role in oral thermosensory coding by driving oro-behavioral responses to cool and warm temperatures. Previous research from our lab showed that TRPM8-mediated thermal input

establishes a neural coding breakpoint in trigeminal pathways, separating cool and warm temperature oral sensory processing. Our lab found that TRPM8-deficient mice, unlike wild-type B6 mice, exhibited behavioral generalization between mild cooling and warmth, displaying warmth-like oro-sensory responses to mild cool temperature water in a temperature-controlled brief-access licking test. However, the influence of TRPM8 in thermosensory effects on taste preference remains unclear. Therefore, we aim to examine the role of TRPM8 function during oral thermosensory-guided licking behavior and its influence on taste preference. In preliminary studies, we tested C57BL/6J (B6, n = 4) and TRPM8-deficient (n = 4) mice in brief-access tests with a room temperature concentration series (0, 100, 300, 500, and 1000 mM) of D-glucose and the non-metabolizable glucose analog α-methyl-D-glucopyranoside (MDG). Both mouse lines show concentration-dependent increases in licking to both stimuli ($p < 0.05$). We will next use a thermo-lickometer to compare licking responses to glucose and MDG at cold (15°C) and mild cool (30°C) temperatures, in TRPM8-deficient and wild-type B6 mice. These experiments aim to elucidate TRPM8's role in integrating oral sensory-related thermal and metabolic signals.

238 **Osmotic And Dehydration Challenges Shape Earthworm Behavior In Their Soil Environment.**

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Earthworms crawl along a tightrope balanced between contrasting osmotic challenges. The thin film of moisture covering earthworm epithelium allows them to respire, but it is incredibly sensitive to either dehydration or becoming waterlogged. Similarly, ions essential for homeostasis are scarce in their soil environment but are desiccating in high concentrations. Thus, we hypothesized that the European nightcrawler (*Dendrobaena veneta*) would demonstrate a preference for moderately moist soil and dilute salt solutions while avoiding extremes of moisture or osmolarity. We utilized two behavioral assays to test these hypotheses: a burrowing assay to measure aversion and a 2-choice T-maze paradigm. In the burrowing assay, a worm is placed on a mixture of soil and aqueous solution and, after 10 min, scored as burrowed if the head is under the soil. While we found that % soil moisture (v/w) had a significant effect on burrowing (ANOVA, $p < 0.001$, n=6), there was a wide range of soil moistures (10-40%) where >98% of worms burrowed. We also tested four salts (NaCl, KCl, $NaNO_3$, and NH_4Cl) at increasing concentrations, with and without amiloride pretreatment (n = 3 to 12). A 3-way ANOVA revealed that salt type ($p < 0.001$), concentration ($p < 0.001$), and amiloride treatment ($p < 0.001$) all significantly influenced the burrowing. For the 2-choice paradigm, we designed, 3D printed, and validated a soil-filled inverted T-maze. In our initial experiments, we compared 0-50% soil moisture to 30% soil moisture and found that earthworms significantly preferred >20% moisture (ANOVA, $p<0.05$, n=6). We are continuing to test the earthworm's preference between differing osmotic conditions to better characterize how these animals detect and respond to various osmotic conditions in their soil environment.

240 **Long-Term Sugar Exposure Increases The Consumption For Glucose Over Fructose In Both C57Bl/6J And T1R2+3Ko Mice**

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Schier et al. previously showed that a sugar exposure paradigm selectively increased licking to glucose relative to fructose in mice. Pittman et al. then showed that sugar-exposed mice showed significantly higher neural activity in the NST for glucose but not for fructose or any of the other non-sweet taste stimuli. In this study, we assessed microstructural licking patterns during 23 h exposures to three concentrations (0.316, 0.560, 1.1 M) of glucose and fructose each presented once in three sets across an 18-day long-term exposure paradigm in female and male wildtype (WT) and Tas1r2 plus Tas1r3 genetic knockouts (KO). All mice innately preferred 0.316 M glucose to all other glucose and fructose concentrations with fructose having the lowest consumptions. Across the three exposures, WT and KO males showed similar increased consumption of 0.316 and 0.56 M glucose but only KO males increased consumption of 1.1 M glucose. In contrast, KO females showed higher consumption for each glucose concentration than the WT females with consumptions increasing across the three exposures. Fructose was the least consumed; however, WT males consumed more fructose than KO males. In contrast, WT and KO females showed similar consumption patterns for fructose that increased for 0.316 M fructose from the first to the second and third exposures with no change in consumption of 0.56 or 1.1 M fructose across the three exposures. Increases in the number of meals rather than the number of licks within the meals appear to account for the differences in consumption. In summary, there are both genotypic and sex differences in consumption of glucose and fructose across an 18-day exposure paradigm. Additional microstructural analysis of licking patterns will be explored in the poster.

242 **Taste Changes In A Rat Model Of Spinal Cord Injury: Impact Of High Fat Diet And Weight Loss Surgery**

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Approximately two-thirds of spinal cord injured (SCI) individuals become overweight or obese. Weight loss/metabolic surgery, including sleeve gastrectomy (SG) is regarded as highly effective in the long-term treatment of obesity and remission of type 2 diabetes. It is, however, unknown if obese individuals with SCI respond to obesogenic diets and SG similarly to the non-SCI. To investigate that, male Wistar rats received either contusion injuries of the spinal cord (T3) or sham operations. After full recovery, all rats were fed a high energy, high fat diet (HFD, 60%kcal from fat) for 6 weeks prior to SG. Taste preferences based on oral and post-oral

effects were assessed using brief-access (10-s) lick rate analysis and long-access (24hrs) two-bottle choice (2BC) tests for various tastants, at various time points. Pre-HFD, SCI compared to sham-surgery significantly reduced lick responses (total licks and bout licks) for sucrose (0.6-1.5M) and increased for sodium chloride (0.01-0.06M) but did not alter 2BC preferences. HFD resulted in greater adiposity in SCI rats and an overall increased lick response to sucrose. Lastly, SG reduced sucrose preferences in both SCI and sham-surgery cohorts with the SCI rats being more sensitive to this effect. cFos IHC revealed significantly greater neural activity to oral sucrose stimulation in the rostral area of the nucleus of the solitary tract in SCI rats that received SG compared to non-SCI SG controls. These findings collectively support the hypothesis that SCI may result in altered taste functions, and in turn, may increase the risk for development of diet-induced obesity. Furthermore, these findings represent the first evidence suggesting that SG may restore normal sweet preferences in SCI with concurrent obesity more efficiently than non-SCI obese subjects.

244 **Taste-Taste And Cross-Modal Interactions In A Real Food System**

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In model systems, sweetness and sourness show mutual mixture suppression, but only at high intensity. Prior work in model systems and real foods show cross modal interactions between taste and smell. Here, we leveraged temporal data from a study using commercial gummy confections to test for these types of interactions in a real food. Pre-screened participants (n=148-156) attended two sessions 7 days apart, evaluating the same samples using two different temporal methods; only the discrete time intensity (dTI) data were used here. Four commercially available gummy confections were used: two were gelatin-based and two were starch-based, and one of each gel system was the regular version, while the other was the extra sour version. Participants evaluated sour, sweet, bitter, drying, chewy, and fruity intensity every 15s over 90s. Smoothed temporal curves and scaffolding parameters (i.e. Imax, AUC, etc.) were calculated for each participant, sample, and attribute. Sweetness Imax values did not differ between 3 of the 4 gummies, but one gummy was significantly less sweet. Imax for sourness showed a different pattern: the two sour versions were more sour than the regular ones, as expected, but one of the two sour gummies was more sour than the other sour gummy. Notably, the most sour gummy was also the least sweet, in agreement with Keast and Breslin's claim that mutual mixture suppression of sweet and sour is intensity dependent. Separately we observed fruity ratings closely mirrored the sweetness ratings and not the sourness ratings, as expected from prior work on minty flavor release in gum. Imax ratings for fruitiness were lowest in the most sour gummy. Collectively, this work suggests patterns seen in model systems can be recapitulated in real worlds with careful psychophysical testing.

246 **Odor Specific Activation Patterns In The Human Olfactory Bulb Detected By High Resolution Bold Fmri On 7 Tesla**

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Most knowledge of the human olfactory system is based on rodent studies,despite interspecies differences.In rodents, a tight correspondence exists between olfactory bulb (OB) glomeruli and sensory neurons,but this organization may differ in humans,who have more glomeruli and sensory neuron types.Human OB activation patterns during olfactory stimulation remain largely unexplored due to limited neuroimaging techniques.Recently, our group demonstrated that T2-prepared BOLD fMRI at 7T reliably measures functional activation in the human OB.This study evaluates whether this method detects odor-specific activation patterns.Five healthy volunteers(25.3±3.3yr; UPSIT 37±2) underwent 7T MRI with two odorants: phenylethyl alcohol(Odor 1) and ethyl hexanoate(Odor 2). Odorless mineral oil served as a control. A custom olfactometer delivered stimuli. 6 ROIs, including the OB, piriform cortex, and other secondary olfactory cortex, were analyzed with 0.5 mm 3D T1w, 0.4 mm 3D T2w, and 1.5 mm T2prep BOLD fMRI. Functional activation was assessed using the Kolmogorov–Smirnov test, and relative signal changes (ΔS/S) were calculated. Robust activation was detected in all ROIs. The OB showed greater ΔS/S than other ROIs, though its time courses were noisier. Odor 1 produced fewer activated voxels and lower ΔS/S than Odor 2. OB activation patterns differed, clustering anteriorly for Odor 1 and posteriorly for Odor 2. Habituation effects were insignificant. This pilot study shows that T2prep BOLD fMRI can detect odor-specific patterns in the human OB, overcoming challenges of small size and susceptibility artifacts. Human OB variability, with blended layers and subject-specific differences, complicates findings. Further validation is needed, but this approach holds promise for mapping individual OB activation patterns.

248 **In Vivo Dynamics Of Dopaminergic Circuits In The Mouse Olfactory Bulb**

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The olfactory bulb (OB) does more than just relay sensory information to the rest of the brain. OB activity is shaped by external and internal signals, like arousal, reward expectation, and perceptual demands. Remarkably, odor-evoked OB activity becomes sparser as task demands transition from coarse to fine odor discrimination. Such context-dependent flexibility might seem surprising for a "primary" sensory region, but it allows for need-driven optimization of perception. The mouse OB offers an accessible model for examining mechanisms of

flexible odor encoding. In particular, OB dopamine (DA) neurons, characterized by the expression of tyrosine hydroxylase (TH), modulate odor discrimination and receive direct synaptic inputs from the basal forebrain (BF), a major source of top-down regulation in the brain. To determine the extent to which context-dependent odor discrimination relies on OB DA neurons, we are using in vivo two-photon imaging to quantify the spatial-temporal dynamics of DA release in the OB as mice perform a context-dependent odor discrimination task. Preliminary results confirm that head-fixed mice learn to rapidly transition between coarse and fine odor discrimination in a head-fixed two-alternative forced choice task. Simultaneously, using a high field number resonance scanning two-photon microscope, we can image the entire dorsal surface of both OBs in awake behaving mice with high spatial-temporal resolution. We have successfully imaged the genetically encoded calcium sensor jGCaMP8f expressed in the OB of TH-Cre mice, and we aim to compare two genetically encoded dopamine sensors, GRAB-DA and dLight. Our results will help us better understand the neuromodulation of olfaction and the neural circuits behind flexible stimulus encoding.

250 **Odor Concentration And Perceived Odor Intensity Processing Within And Between The Human Olfactory Bulb And Piriform Cortex**

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Odor intensity plays a key role in how humans perceive and interpret their surroundings. In several species, neural oscillations have been linked to odor concentration processing with evidence suggesting that the oscillation amplitude is modulated by the strength of odor concentration. However, no studies have explored whether oscillatory activity in the human olfactory bulb (OB) and piriform cortex (PC) is related to odor concentration and how it differs from perceived odor intensity. To this end, we recorded odor-dependent neural activity using EEG in the OB and PC of human participants while collecting trial-by-trial intensity ratings. Our findings show that no information regarding odor concentration is transmitted between OB and PC through oscillatory activity. Instead, perceived intensity is processed in a bottom-up fashion in the OB gamma band 200 ms after odor delivery, then transmitted to the PC via gamma oscillations for further processing. To better understand the relationship between odor intensity processing, cognition, and neural oscillations, we then analyzed burst activity in the beta and gamma bands. We found that odor concentration predicted OB and PC beta burst behavior, but results did not survive cluster correction. In contrast, for perceived intensity, we found significant gamma burst activity in the OB around 800-1100 ms, coinciding with significant beta burst activity in the PC during the same period. This timing matched the one found in the coherence spectrum, during which top-down information from the PC conveys refined information back to the OB in the beta band. The late timing of activation, with converging evidence across analyses, suggests that perceived intensity is mainly regulated by top-down information.

252 **Human Olfactory Bulb Beta Activity Predicts The Gamma Activity Of The Following Sniff**

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Between the human olfactory bulb (OB) and the piriform cortex (PC), gamma and beta bands have been shown to communicate odor identity, valence, and intensity. Early gamma activity is directed from the OB to the PC, while later beta activity has been shown to carry information communicated back from the PC to the OB. We hypothesized that the feedback conveyed through the beta band informs the gamma band in the OB with information regarding the just experienced odor to influence processing of the following sniff. To evaluate this, we conducted a study with 40 participants where odor delivery was initiated at the beginning of the first sniff and remained until one second after the second sniff. Neural recordings were collected using EEG and source reconstruction was employed to extract the neural time course in the OB. We related the power spectrum of the beta band activity in the OB during the first sniff to gamma band activity during the second sniff through a mixed-effects model, controlling for baseline beta activity. The results show that stronger beta power during the first sniff predicts stronger gamma power during the second sniff. This suggests a connection between beta activity in the first sniff and gamma activity in the second sniff.

254 **Analyzing The Role Of Cd11B And Microglia In Recovery From Olfactory Injury**

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Olfactory sensory neurons are constantly turning over; dead neurons are being engulfed and cleared, while newly differentiated neurons arise from stem cells. This neuroregeneration is facilitated by several cell types, including microglia and olfactory ensheathing cells. Here we focus on microglia, the immune cells of the CNS. Microglia show a robust response to injury and pathogens, moving towards the site of injury to respond through phagocytic and anti/pro-inflammatory pathways. Previously, our lab found an increase of integrin CD11b in the olfactory bulb (OB) following injury to the olfactory epithelium induced by a methimazole injection. We hypothesized microglia were directly involved in the recovery process in vivo and utilized CD11b-related pathways to respond and facilitate recovery. Using immunohistochemistry (IHC) and behavioral testing, motility of microglia throughout the OB and recovery from injury were analyzed by quantification of Iba1 expression and cell counts in the OB, along with the “Hidden Cookie” behavioral test, in both wild-type (WT) and CD11b-deficient

knockout mice ($CD11b^{-/-}$). For $CD11b^{-/-}$, IHC experiments showed similar movement of microglia through the OB compared to WT, except at 7 days post-injury, which showed higher levels of Iba1 throughout the OBs. Additionally, behavioral data showed a slower functional recovery compared to WT, suggesting microglia's involvement in the process in a time-dependent manner. Also, the differential pace of functional recovery for $CD11b^{-/-}$ mice supports that CD11b is directly involved, and further research is needed into the pathways at work.

256 **Optogenetic Stimulation Of The Olfactory Sensory Neuron Input To The Olfactory Bulb Elicits Gamma Entrainment Of Dorsal Hippocampus In A Mouse Model Of Alzheimer&Rsquo;S Disease**

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Entrainment of the hippocampus in low gamma (40 Hz) oscillation through activation of visual or auditory cortex elicits both neuronal and glial responses that attenuate AD pathologies (Martorell et al. 2019, PMC6774262). Theta frequency-coupled gamma oscillations of the olfactory bulb (OB) are known to entrain gamma oscillation in the hippocampus and are robust in non-disease states. Therefore, it is plausible that the reintroduction of directionally coupled low gamma entrainment of the hippocampus by the OB will also attenuate AD pathologies and will slow the cognitive decline in 5xFAD mice. We are in the process of testing whether 40 Hz optogenetic activation of the input to the OB in OMP-ChR2 mice will attenuate AD pathologies and slow the cognitive decline in 5xFAD mice. Mice were stimulated by 473 nm laser light pulses targeting the olfactory epithelium continuously for 1 hr in at 40Hz. Stimulation was performed in a full cohort of control and 5xFAD mice and C57Bl/6 mice (with or without cross to OMP-ChR2 mice). The local field potential was recorded in both OBs and in both dorsal hippocampi. We find reliable activation of the OB at 40Hz that entrains CA1 in the hippocampus. However, the effect of the entrainment is smaller in the 5xFAD mice compared to C57BL/6. In addition, we are performing two-photon imaging of the calcium indicator GCaMP6f in pyramidal cells in dorsal CA1 in 5xFAD mice. Surprisingly, we find waves of increased calcium crossing the field of view. These waves have not been observed in any of the control mice. We are currently performing experiments to determine whether entrainment along the OB-hippocampus circuit can induce transcription level changes in immune glial cells that result in amelioration of AD pathology.

258 **Heterogeneous Monotonic And Non-Monotonic Responses To Odor In Mitral/Tufted Glomeruli Of The Mouse Olfactory Bulb.**

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Current models of olfactory sensory processing in the olfactory bulb (OB) posit that both intra- and interglomerular inhibitory circuits are involved in transforming incoming sensory input. However, the impact of these circuits on different kinds of olfactory receptor neuron (ORNs) inputs remains poorly understood. We generated a model of the OB input-output transformation in which the output of each glomerulus is a function of its ORN input, local intraglomerular inhibition and interglomerular normalization in which activity of each glomerulus is divided by the population response. The output of the model included linear and non-linear concentration-response relationships that were a complicated function of the input ORN Hill coefficient and affinity. The concentration-response relationships could be broadly categorized into those that either monotonically increased or decreased with increasing concentration, and others that decreased then increased, or increased then decreased. Increasing then decreasing glomeruli required normalization in our model, were present in glomeruli with higher affinity ORN input, and were heterogeneous in their decrease. *In vivo* 2-photon Ca^{2+} imaging from mitral/tufted (MTC) glomeruli in awake mice revealed the presence of glomeruli exhibiting similar response types. Notably, increasing levels of excitation drove higher levels of suppression in subsets of glomeruli. Glomeruli that first increased then decreased were present in nearly half of glomeruli. The sensitivity of individual glomeruli was significantly correlated with the degree to which it was non-monotonic. Our results demonstrate that nonlinear responses of MTC to changes in odor concentration are not unusual, but indeed are typical, and that they can be explained by interglomerular inhibition.

260 **Odor-Specific Increases In Both Sensitivity And Dynamic Range In The Olfactory Bulb Of The Mexican Cavefish**

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Astyanax mexicanus, the Mexican tetra, consists of eyed, river dwelling surface populations (surface fish) and multiple eyeless cave populations (cavefish) which have undergone rapid sensory evolution, and therefore

provide a unique comparative model by which to understand evolutionary processes. The sensory adaptations of the cavefish include eye loss, along with an expansion of the sensory organs and associated brain areas governing taste and smell. Previous studies have demonstrated that cavefish exhibit enhanced behavioral sensitivity to amino acids relative to their surface counterparts. However, the brain areas involved in this altered sensory perception are unknown. We tested the hypothesis that chemosensory adaptation in cavefish is the result of altered functional processing at the first stages of olfactory sensory processing, the epithelia and the bulb. We performed epifluorescence imaging in the olfactory bulbs of transgenic surface and cavefish that express the genetically encoded calcium indicator GCaMP6s in response to select amino acids presented at different concentrations. The functional response threshold of cavefish was 4 orders of magnitude lower in response to the odors alanine and lysine than age-matched surface fish. Other amino acids tested did not elicit differences in response between surface and cavefish. Our results suggest that cavefish sensory adaptations include changes in olfactory sensory processing beginning in the olfactory bulb. Future studies will examine the molecular changes mediating enhanced sensitivity, and behavioral outcomes of this adaptation.

262 **Transcutaneous Vagal Nerve Stimulation In Olfactory Bulb-Relevant Frequencies Modulate Olfactory Function**

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There are few effective treatments for non-conductive olfactory dysfunction. A potential treatment which has shown mixed results is transcutaneous vagal nerve stimulation (tVNS). In mice, VNS stimulates the olfactory bulb (OB) by inhibiting neurons in the periglomerular layers of the olfactory bulb. This could potentially enhance olfactory function by increasing discrimination between signal and background. To date, results have been inconsistent where most studies in human participants demonstrate no effects on psychophysical measures. However, the VNS paradigms used have not been consistent with how the human OB processes odors, leaving uncertainty whether the OB, or the olfactory system, is truly stimulated. Here, we evaluated whether tVNS paradigms that match OB processing frequencies modulate olfactory discrimination performance (pre *vs* post) with a focus on frequencies previously identified as top-down (25 Hz) and bottom-up (55 Hz) processing of odors. In Experiment 1 (n=27), we performed either 20 min tVNS on the left ear cymba conchae region, or earlobe sham stimulation, using a protocol consisting of 25 Hz pulses. We found no difference between tVNS and sham in olfactory performance (p>.48). In Experiment 2 (n=42), we used an identical design but stimulated with 55 Hz. We found that tVNS significantly reduced participants' ability to discriminate between odors compared to when participating in the sham session (p<.001). There was no effect of tVNS on either attention or supra-threshold odor intensity ratings in either of the experiments. This result demonstrates that tVNS likely can modulate OB processing of odors when stimulated in a gamma band frequency that is linked to OB processing of input stimuli.

264 **Olfactory Bulb Inhibitory Interneurons Modulate Threat Perception In Mice**

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Certain threat responses are innate and are genetically predetermined, for example, the fear reaction shown by rodents toward predator scent. TMT (2,3,5-Trimethyl-3-thiazoline) is a volatile sulphur-containing single molecule kairomone derived from fox feces and has been demonstrated to function as a predatory cue to rodents. Exposure to this odor leads to avoidance and freezing responses, indicative of fear. Amygdala plays a crucial role in assigning emotional valence to incoming sensory information, thereby enabling instinctive behaviors such as active exploration, evading predator scents or freezing. Olfactory information is transmitted to various brain regions, including amygdala via projection neurons of the olfactory bulb. The inhibitory interneuronal population modulates the spiking activity of excitatory projection neurons (Mitral/Tufted cell) and helps refine the odour percept. Although the Amygdala and Periaqueductal Gray (PAG) have been demonstrated to be crucial in eliciting defensive behaviors and mediating transitions between fight, flight, and freezing responses, the role of the pre-cortical circuitry remains largely unexplored. Here, we define defensive behaviors of increased freezing and escape attempts in response to TMT, using a combination of Deeplabcut, SimBA, and Bonsai. The in vivo calcium imaging from GAD-65-expressing OB interneurons revealed higher population activity in response to TMT, compared to volatile esters and ketones. The optogenetic modulation of the same interneuron population resulted in a bidirectional shift of the defensive behavioral readouts, confirming the role of OB inhibitory network in modulating threat perception.

266 **The Persistence Of Changes In Olfactory Bulb Taar4-Related Circuits Evoked By Early Postnatal Exposure To Phenethylamine (Pea) Following Olfacotry Sensory Neuron Ablation**

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Critical periods are essential for proper development of mammalian sensory circuits. In the mouse olfactory system there is an early postnatal critical period during which errors in glomerular map formation can be corrected. Furthermore, critical period exposure can alter the valence of innately recognized odorants. Mice exposed during the olfactory critical period to the innately aversive odorant phenethylamine (PEA), detected by olfactory sensory neurons (OSNs) expressing the trace amine-associated receptor 4 (TAAR4) do not demonstrate stereotypical innately avoidant behaviors, but rather are attracted to PEA. This change in behavior is accompanied by an increase in the number of TAAR4 glomeruli per OB. Here, we seek to address two key

questions: how neonatal PEA exposure alters the odor responsiveness of OB output neurons, and whether the changes in valence toward PEA persist following complete OSN ablation and subsequent reinnervation. To address the first question, we injected mice with AAV5-syn-GCaMP6s to record PEA-evoked calcium responses in mitral and tufted cells using in vivo 2-photon microscopy. To address the second question, PEA-exposed mice underwent repeated odor preference testing to determine whether the shift in innate valence persists following methimazole (MMZ)-mediated OSN ablation and subsequent repopulation. While we did not see a difference in OB output neuron activity after neonatal PEA exposure, repeated odor preference testing revealed that the preference for PEA does not recover six weeks after MMZ treatment. These data suggest that OB circuitry may reorganize after large-scale OSN ablation and regeneration.

268 **Olfactory Bulb Theta Oscillations In The Absence Of Theta-Range Sniffing**

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In rodents, olfactory bulb theta oscillations (4–12 Hz) are largely locked to fast, theta-range sniffing rhythms. As a result, olfactory neural representations are defined by sniffing, which provides a temporal framework for odor processing. Rodent sniffing behavior is dynamic, modulated by learning and behavioral state, and directly impacts temporal processing windows in the olfactory system. Thus sniffing provides a direct link between behavior and neural activity, and is an integral aspect of odor coding mechanisms in the brain. Despite the fundamental link between sniffing behavior, theta oscillations, and neural representations of odor in rodents, the presence and function of theta oscillations in the human olfactory bulb remain uninvestigated. Human olfactory processing occurs under vastly different temporal constraints: humans sniff at rates far slower than rodents, raising questions about the applicability of these principles to human olfactory circuits. Since rodent studies demonstrate a direct relationship between sniff-driven oscillations and neural coding, the absence of theta-range sniffing in humans necessitates research into whether the human olfactory bulb operates under similar mechanisms. Without rhythmic sampling in the theta range, does the human olfactory bulb still generate theta oscillations that create a temporal structure for odor responses? Here we will explore this question by combining olfactory bulb recordings with sniffing tasks in humans. Preliminary results from 4 participants suggest that both intentional sniffing and odor drive theta oscillations in the human olfactory bulb, and that this theta rhythm organizes a strikingly consistent, odor-induced gamma oscillation centered around 54 Hz.

270 **Behaviorally Relevant Features Of The Neural Code In Olfactory Bulb**

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Odor stimuli evoke spatiotemporal patterns of activity at the glomerular level in the olfactory bulb. The relationship between patterns of neural activity and perceptual similarities among sensory stimuli remains debatable. In this study, we designed an experiment using the 2-alternative-forced-choice (2AFC) paradigm to measure the generalization ability of mice in precise odor discriminations. This task allowed us to smoothly vary the spatiotemporal patterns of activity using three-component odor mixtures to identify the relevant features of neural activity that drive behavioral discriminations. We trained mice to discriminate a specific mixture of three odors (referred to as the "Target") from a range of different odor stimuli (referred to as "Non-Targets"). In subsequent probe trials, we manipulated the mixture's composition to test the mice's ability to generalize their response. We then employed two-photon Ca2+ imaging to measure the neural activity in glomeruli in mice expressing the fast calcium indicators in olfactory sensory neurons. Based on these recordings, we developed a model to identify the critical features of neural activity that influence behavior. Our analysis suggests that the most relevant glomeruli are activated within the early temporal window of the sniff cycle. The weight of the relevant glomeruli in the model decays over the temporal window of the sniff cycle, and not all glomeruli active during this early phase are behaviorally relevant. Furthermore, we showed these observations are generalizable across diverse odor sets. These findings provide valuable insights into how the olfactory system represents and distinguishes between odor mixtures, highlighting the importance of the order of neural activity and the significance of temporal dynamics in encoding these mixtures.

272 **Genetic Identification Of A Rapidly-Adapting Low-Threshold Mechanoreceptor Innervating Fungiform Papillae**

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Mechanosensory neurons detect the location and textures of food. Here, I reconstructed the peripheral axon of tongue-innervating *Pvalb*+ to determine anatomic receptive field size and used optotagging and electrophysiology to examine *Pvalb*+ neuron function. Functional responses from *Pvalb*+ neurons were compared to the full population of low threshold mechanosensory neurons (LTMRs) that innervate the tongue. I found that *Pvalb*+ neurons have a small anatomical receptive field, limited to a rough area between 3800 μm2

and 6000 μm2, which is roughly the area of one or two fungiform papillae. Functionally, the *Pvalb*+ population consisted of only rapidly-adapting neurons while the full population of LTMRs contains both rapidly-adapting and slowly-adapting LTMRs. When we compared the spike rates of *Pvalb*+ neurons to the slowly-adapting neurons of the full population, we found that unlike slowly-adapting neurons, *Pvalb*+ neurons did not increase their spike rates to increasing forces. We then determined the conduction velocity of *Pvalb*+ neurons compared to the full population of LTMRs. While we found that the full population of LTMRs had a wide range of conduction velocities (C-fibers, A-slows, and A-fasts), all of the *Pvalb*+ neurons fell into the A-fast category. When we tested for chemical detection using high concentrations of salt and citric acid, we found that the *Pvalb*+ did not respond. Similarly, when we tested *Pvalb*+ neurons for temperature sensitivity using a temperature ramp in both the warming and cooling directions, *Pvalb*+ neurons were insensitive to temperature. These findings show that *Pvalb*-expression identifies a tongue-innervating genetic subtype with specific functional properties that is well-suited to provide information of location and texture of food in the oral cavity.

274 **Olfactory-Trigeminal Interactions In Parkinson'S Disease Compared To Others Forms Of Olfactory Dysfunction**

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Olfactory dysfunction (OD) is a common early symptom of Parkinson's disease (PD), but is not specific to this condition, as approximately 20% of the general population also experience various forms of OD. Distinguishing PD-related OD from non-Parkinsonian OD (NPOD) is crucial for the use of olfactory measures in early screening. In this context, the trigeminal system—a chemical sense involved in the perception of freshness, pungency, pain, tickling, and burning when exposed to odorants—is of particular interest due to its close interconnection with the olfactory system. These systems suppress and/or enhance each other, and this interaction appears specifically altered in PD compared to NPOD. To better understand these interactions, our study evaluated how olfactory co-stimulation influences the localization of a pure trigeminal stimulus (CO_2) in 18 PD patients, 20 NPOD patients, and matched control groups with a normal sense of smell. We used an olfactometer to deliver stimuli under four conditions: a lateralization test with pure CO_2, with pure phenyl ethanol (PEA), with ipsilateral co-stimulation of CO_2 and PEA in the same nostril, and with contralateral co-stimulation of CO_2 and PEA in opposite nostrils. Brain activity was recorded using electroencephalography (EEG). Ipsilateral, but not contralateral, olfactory co-stimulation with a pure odorant improved the ability to localize a trigeminal stimulus in all groups ($p<0.05$). Ongoing analyses of evoked potentials will further explore these interactions at the central level. To conclude, the presence of PEA facilitates trigeminal responsiveness.

276 **Examining Orthonasal And Oral Trigeminal Receptor Activation And Role In Spicy Food Preferences**

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Most of the literature on the relationship between human food preferences and sting has focused on oral TRPV1 activation, despite the fact that the trigeminal nerve branches widely and includes several receptor types. The present within-subjects designed study examined frequency of spicy food consumption (FFC) based on personality (extraversion, food neophobia, sensation seeking), receptor type, and stimulus properties (familiarity, edibility, intensity, likeability) in response to both orthonasal and oral stimuli. Capsaicin (TRPV1) was delivered to participants orally, while cinnamaldehyde (TRPA1), camphor (TRPV1), eucalyptol (TRPM8), and vanillin (Non-Trigeminal practice) were delivered orthonasally. Principle component analysis was performed on the 3 items that compose the FFC scale. The first principle component (Spicy PC) accounted for 83% of the variance across items; this component (scaled and centered) was used as thedependent variable in a stepwise backward regression that included SS, extraversion, food neophobia and their interactions as predictors. The resultant model included only the novelty subscale of the sensation seeking personality, ($t(90) = 2.970$, $p = .004$); No other personality factors or psychophysical ratings entered the model. Sensation Seeking Novelty subscales were correlated inversely with food neophobia and extraversion. Thus, self-reported spicy food consumption was related to novelty aspects of sensation-seeking personality, though it was unrelated to psychophysical ratings of the trigeminal stimuli in the present experiment.

278 **The Examination Of Oral Astringency With Edible Film Formulations**

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Astringency is defined as a chemosensation that induces puckering, tightening sensations, and/or drying sensations on the tongue and membranes of the oral cavity. Astringency is attributed to high tannin levels that occur in unripened fruit, cranberries, and some red wines. Oral astringency is generally analyzed by adding phenolic compounds such as tannic acid or salts such as aluminum sulfate (alum) to aqueous solutions. In this study, tannic acid was incorporated within rapidly dissolving edible films to assess astringency. Edible films that contained either 2 or 4 micromoles of tannic acid were prepared by adding plasticizers to the film solution, sonicating the film solution, and drying the solution at room temperature. The general Labeled Magnitude Scale was used to measure overall (side taste) intensities and dryness/puckering intensities. Maximal intensities for both amounts of tannic acid occurred 30 seconds after the films dissolved, and peak intensities were in the moderate range. The most commonly reported side tastes were bitter, sour, or no discernible taste. Mean hedonic scores obtained from a bipolar hedonics scale were in the moderately dislike range. Average dryness/puckering intensities were in the weak range for tannic acid films that contained 2 micromoles, and in the moderate range

for 4 micromole films. Tannic acid-salivary protein interactions, and the precipitation of these complexes may cause oral astringency. To test this hypothesis, egg albumin was added to tannic acid films. This additive resulted in a small decrease in mean intensities and a delay in reaching maximal intensities. In summary, edible films are useful for identifying astringency in the absence of water, and provide an improved delivery method for measuring astringency and its causes in the oral cavity.

280 **Differentiating Neural Responses To Olfactory And Trigeminal Stimuli Using Eeg And Machine Learning**

Johannes Frasnelli[1,2] , Matin Asghar Pour[1], Olivier Fortier-Lebel[1], Sarah Brosse[1], Emilie Hudon[1], Anne-Lise Saive[3], Jie Mei[4]

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Chemosensory stimuli generate spatially distributed neural representations observable with EEG. Most odorants activate both olfactory and trigeminal systems. This study tested the hypothesis that olfactory (phenyl ethanol, PEA), trigeminal (Eucalyptol, EUC), and mixed stimuli (Ipsilateral/Contralateral PEA and EUC) elicit distinct EEG patterns, measurable via event-related potentials (ERPs) and classifiable with machine learning. EEG data from 31 healthy participants were recorded using 32 electrodes. Participants underwent 40 trials per condition, with data preprocessed via band-pass filtering (1–45 Hz), ICA for artifact removal, and segmentation into -200ms to 2 s epochs. Key ERP components included P1 (early sensory processing) at 0.210–0.220 s in frontal channels (Fz, F3), N1 (attention-related) at 0.344–0.370 s in parietal regions (Pz, CP6), and P2 (cognitive processing) at 0.520–0.696 s in central-parietal channels (Cz, CP2). Significant differences were observed between PEA and EUC conditions ($p = 0.001$), PEA and Contralateral conditions ($p = 0.011$), and Ipsilateral and Contralateral conditions ($p = 0.037$), suggesting specific sensory interactions. A random forest algorithm classified conditions, achieving 81% accuracy for PEA vs. Ipsilateral stimuli and 68–73% for other conditions. These results demonstrate machine learning's efficacy in distinguishing chemosensory stimuli from EEG data. In conclusion, this study highlights distinct neural mechanisms for olfactory and trigeminal stimuli and the potential of EEG-based machine learning for chemosensory classification.

282 **Capsaicin Sensitization During Consumption Of A Real Food Is Non-Linear**

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Prior work in model systems indicates the amount of oral burn evoked by capsaicin, a TRPV1 agonist found in chili peppers, increases monotonically with repeat acute exposure, increasing by nearly ~52% over 10 trials when applied to the tongue via cotton swab. However, this does not match lived experience during eating, so we investigated capsaicin sensitization using a real food. After orientation to a generalized Linear Magnitude Scale and a generalized Bipolar Hedonic Scale, 75 participants received a series of 10 identical chicken tikka masala samples containing hot Hungarian paprika sequentially. Samples were served every 30 seconds and participants were instructed to consume each 15 g sample in its entirety before rating oral burn intensity and liking. Random coefficient models revealed a curvilinear relationship between repeated exposure and burn. Specifically, with each additional sample consumed, burn increased ($p<0.001$), but this trajectory had a negative quadratic coefficient ($p=0.002$), indicating a plateau with additional exposure. Hedonic trajectories differed from burn intensity, dropping across exposures ($p=0.01$). This may reflect a simple effect wherein liking dropped as burn increased outside an optimum range, but we cannot rule out the well-known phenomenon of sensory-specific satiety. Here, we build on previous findings in model systems indicating capsaicin sensitization increases burn monotonically, by showing that oral burn during eating has a quadratic trajectory characterized by initial sensitization within the first few trials, followed by a plateau. This discrepancy may relate to locus or size of stimulus field (small loci on the tongue via cotton swab versus whole mouth during naturalistic eating) or tongue movement (static versus dynamic).

284 **Identifying Mechanisms Of Astringency Transduction**

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Astringency is defined as a dry, rough, and puckering sensation that is associated with phenolic compounds, known as tannins, that are present in many plant-based foods. Astringency sensation depends on the activation of trigeminal neurons, suggesting that transduction depends on somatosensation rather than taste. Chemosensory and mechanical mechanisms of phenolic compound transduction have been proposed, with evidence supporting both mechanisms. Using a combination of calcium imaging and brief access preference testing behavioral assays, our data suggests that a mechanosensory subpopulation of trigeminal neurons are activated directly by tannic acid through chemotransduction, providing a potential mechanism for astringency sensation. Preliminary *in vivo* calcium imaging suggests that trigeminal mechanosensory neurons that respond to tannic acid are responsive to stroking but not pressure, a response profile that is highly represented by a subpopulation of trigeminal neurons labelled by Vglut3. We found that 40% of Vglut3^{lineage} neurons respond to tannic acid *in vivo*, suggesting that Vglut3^{lineage} neurons may be involved in transduction of tannic acid. Through *in vitro* calcium imaging we have found that tannic acid responsive neurons are enriched in the Vglut3^{lineage} subpopulation and respond in the absence of mucosa and saliva, indicating that epithelial intermediates are not required for astringency transduction. Our behavior assays show that while astringency aversion is only mildly affected by olfaction and

taste, selective inhibition of Vglut3^{lineage} neurons reduces aversion to tannic acid. Collectively, our results suggest a role for Vglut3^{lineage} neurons in astringency transduction and sensation.

286 **Determining The Contribution Of Intranasal Chemesthetic Sensation On Addiction.**

Maria F. Ramirez[1], Abhishek Gour[2], Emma K Watson[1], Abhisheak Sharma[2], Daniel Wesson[1]

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Chemosensory cues are instrumental in guiding motivated behaviors and affective states. Not surprisingly, many drugs of abuse are chemosensory rich. Cocaine, in addition to its psychostimulant effects on the dopaminergic system, also evokes nasal sensation upon inhalation. The mechanisms underlying sensation of cocaine and how it may impact cocaine abuse liability are both unknown. Here we report the development of a reliable surgical implant which permits access to the nasal epithelium of freely behaving mice for intranasal delivery of cocaine with precise control over volume and therefore dosage of drug. First, we validated that intranasal infusion of cocaine rapidly results in detectable levels of drug in the plasma and brain. Next, utilizing canonical behavioral assays of drug response, we found that cocaine-infused mice display hyperlocomotion within minutes post-infusion and exhibit instrumental responding for cocaine. Specifically, mice extended effort to acquire cocaine intranasally when engaged in an intranasal drug self-administration paradigm, with some mice displaying strong responding to nose poke in a cocaine-associated port, in the absence of any other sensory cues. Furthermore, we observed a sneeze response and facial-grooming behavior evoked rapidly upon delivery of intranasal cocaine, suggestive of the sensory response induced by cocaine agonism. Currently, we are investigating the sneeze reflex induced by intranasal drug delivery in combination with simultaneous monitoring of brain dopamine dynamics to unravel the role of intranasal chemesthetic sensation in directing drug seeking. Together, this work begins to establish a pre-clinical paradigm to investigate the role of chemosensation in the perceptional qualities of drugs of abuse.

10:00 - 11:00 AM	Calusa EFGH
Diversity, Equity, Inclusion, and Belonging (DEIB) Lecture	

10:00 **You Are Whole Just As You Are: More To Inclusion Than Widening The Door**

Dr. Deana McDonagh[1,2,3]

[1]Professor of Industrial Design (School of Art + Design), [2]Director of the (dis)Ability Design Studio (Beckman Institute), [3]Health Innovation Professor (Carle Illinois College of Medicine)

11:00 - 12:00 PM	Calusa EFGH
Membership Business Meeting	

Get involved! Join us for reports from the society leadership on the state and future of the association. All members are welcome and encouraged to attend.

12:00 - 3:00 PM	Lunch On Own
Free Time	

3:00 - 4:00 PM	Great Egret
Journal Club: History of assessing ligand sensitivity and selectivity of odorant receptors	

This year's Journal Club will highlight the evolution of methods utilized to assess the physiological role and function of odorant receptors since their discovery in 1991 by Buck and Axel.

We will start by reviewing Zhao et al.'s 1998 paper, "Functional expression of a mammalian odorant receptor," in which the authors accomplished rat I7 receptor expression in its native environment, the olfactory sensory neuron, via recombinant adenovirus. The authors found this receptor is selective for C7 to C10 saturated aliphatic aldehydes although they did not resolve how those odorants physically interact with receptor binding sites. However, this and other expression approaches launched decades of additional work to identify ligands for the family of odorant receptors.

While much progress has been made, a recent review by Lalis et al observed that a ligand has not been identified for approximately half of the known receptor variants. Thus, our discussion will include the 2024 paper by de March et al. "Engineered odorant receptors illuminate the basis of odour discrimination," and its application of cryo-EM to the long unresolved problem of describing odorant receptors protein structure. This exciting advancement furthers our understanding of the molecular determinants of ligand selectivity and will enable further deorphanization via in silico methodologies.

AGENDA

- Introduction (Jessica H. Brann, Ph.D., dsm-firmenich, New York, NY, USA)
- Classic publication: Functional expression of a mammalian odorant receptor - PubMed (Ricardo Araneda, Ph.D., University of Maryland, College Park, MD, USA)
- Recent publication: Engineered odorant receptors illuminate the basis of odour discrimination - PubMed (Mona Marie, Ph.D., Molecular Genetics and Microbiology Department, Duke University School of Medicine, Durham, NC, USA)

4:00 - 6:00 PM	Estero Ballroom
Poster Session IV	

201 **Unveiling The Sulfur Scent: The Impact Of Copper Metabolism On Olfactory Dysfunction In Wilson'S Disease**

Shania Appadoo[1], Mona Marie[1], Maira H. Nagai[1], Martina Ralle[2], Hiroaki Matsunami[1]

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[2]Department of Biochemistry and Molecular Biology, Oregon Health & Science University, Portland, OR, United States

Wilson's disease (WD) is a genetic disorder caused by mutations in the copper transporter ATP7B, resulting in toxic copper accumulation in the brain and liver. Notably, WD patients often exhibit specific anosmia,

particularly for sulfur-containing odorants such as skunk spray and tert-butyl mercaptan (TBM), the odorant added to natural gas. This unique symptom hints at a potential link between copper metabolism and olfactory function, a connection that remains poorly understood. Using an ATP7B constitutive knockout mouse model of WD, our findings support the hypothesis that copper is essential for detecting sulfur-containing odors *in vivo*. Olfactory neurons expressing odorant receptors (ORs) responsive to TBM exhibit robust activation in wild-type mice but not in ATP7B knockout mice. Copper levels are dramatically reduced in the olfactory epithelium of ATP7B knockout mice, and ATP7B is expressed in a subpopulation of olfactory cells. To further investigate the local effects of ATP7B deletion on copper homeostasis and olfactory neuron function, we generated cell type-specific ATP7B knockout mice using Ascl3-Cre mouse strains. In this model, no significant differences in copper levels in the olfactory epithelium were observed between wild-type and ATP7B conditional knockout mice. Additionally, olfactory neurons expressing Or2t48 were activated by TBM in both wild-type and ATP7B conditional knockout mice. This study advances our understanding of how copper metabolism impacts sensory systems, particularly olfactory function. Furthermore, it emphasizes the translational potential of olfactory biomarkers in diagnostics and therapeutics.

203 **Persistent Chemosensory Dysfunction After Covid-19 And Its Associations With Quality Of Life And Eating Behaviour: The Covorts Study**

Birgit van Dijk, Sanne Boesveldt
1Division of Human Nutrition and Health, Wageningen University & Research, Wageningen, Netherlands

Knowledge on how persistent COVID-19-related chemosensory dysfunction affects quality of life and eating behaviour over time is lacking. The COVORTS cohort included 76 patients within 3 months of COVID-19 infection who self-reported smell dysfunction >1 month. For one year, patients filled in monthly questionnaires on quality of life, eating behaviour and self-reported chemosensory function, and olfactory and gustatory function was psychophysically measured every three months. The first aim of this analysis was to assess whether the associations between quality of life, eating behaviour and measures of chemosensory function change over time. The second aim was to evaluate whether it is possible to predict patients' quality of life and eating behaviour at 1-year follow-up based on the measures taken at baseline. Quality of life was measured by the English olfactory disorders questionnaire (eODQ). Appetite and hunger ratings were measured by the Appetite, Hunger, and Sensory Perception questionnaire (AHSP). Using best subsets regression, we observed that both psychophysical and self-reported measures of chemosensory dysfunction were common predictors of our outcome measures, and that those predictors change between baseline and 1-year follow-up. For example, total Sniffin' Sticks score and self-reported trigeminal functioning were common predictors for one of the eODQ outcomes at baseline, but no longer at 1-year follow-up. Instead, the Identification dimension of the Sniffin' Sticks and parosmia were common predictors. These results will next be used to create a prediction model for the outcome measures at 1-year follow-up, based on the measurements collected at baseline. The results of this study will provide further insight in the burden of persistent COVID-19-related chemosensory dysfunction.

205 **Relation Between Olfactory Cleft Findings And Ph In Olfactory Dysfunction Patients**

Rumi Sekine[1,2], Eri Mori[2], Yuji Kishimoto[2], Monami Nagai[2], Masayoshi Tei[2,3], HIrotaka Tanaka[2,4], Nobuyoshi Otori[2]

[1]1. Department of Otorhinolaryngology, St. Luke's International Hospital,, Tokyo, Japan, [2]2. Department of Otorhinolaryngology, The Jikei University Hospital, Tokyo, Japan, [3]3. Department of Otorhinolaryngology, The Jikei University Katsushika Medical Center, Tokyo, Japan, [4]4. Department of Otorhinolaryngology, The Jikei University Kashiwa Hospital,, Chiba, Japan

Background: Olfactory dysfunction (OD) can arise from aging, chronic sinusitis (CRS), and other factors affecting the olfactory cleft (OC) homeostasis. We have investigated that OD patients have significantly higher OC pH than normal subjects, suggesting that OC homeostasis is disrupted in patients. This study aims to investigate the factors associated with the change in OC pH including CT findings. Methods: We recruited patients with subjective OD, conducting general medical history taking, card type odour identification tests (OE), T&T olfactometry, general ENT examination and sinus CT scans. OC opacity was scored (0–5) by every 25 percent, and the Lund-Mackay (LM) scores of ethmoidal sinuses were recorded. Finally, a digital pH sensor catheter was placed at OC, middle turbinate (MT), middle meatus (MM) and each pH were recorded. Statistical significance was determined by Spearman's rho ($p<.05$). Results: Among 50 patients (20 CRS-OD, Others ; 20 PVOD 8 PTOD, 2 idiopathic), OC pH correlated with MT/MM pH in CRS-OD and Others ($p<0.001$), age and OD severity was also correlated in CRS-OD (Age $\varrho=36$, $p=0.021$, OE $\varrho=-0.41$, $p=0.015$; T&T threshold $\varrho=0.39$, $p=0.21$; VAS $\varrho=-0.65$, $p<0.001$), but not with Others (Age $\varrho=-0.21$, $p=0.374$, OE $\varrho=-0.11$, $p=0.421$; T& T threshold $\varrho=-0.03$, $p=0.838$; VAS $\varrho=-0.23$, $p=0.084$). Neither OC opacity nor LM scores correlated with pH or OD severity in both CRS-OD and Others. Conclusions: This study showed that CT findings were not related to OC pH, which was contrary to our expectations. However, elevated OC pH was significantly associated with severity of OD with CRS, highlighting the role of OC environmental damage in conductive OD. These results suggest that mucus components or some other different condition in the OC might play a critical role in OD, warranting further investigation.

207 **Specific Associations Exist Between Olfactory And Cognitive Deficits In Adults With Post-Covid Persistent Olfactory Dysfunction: A Scent For Long Covid Baseline Analysis**

Nicole M Cash[1], Mary Clare M Koebel[1], Lisa M McTeague[1,2], Bashar Badran[1], Aicko Y Schumann[1], Thomas W Uhde[1], Rodney J Schlosser[3], Bernadette M Cortese[1]

[1]Department of Psychiatry and Behavorial Sciences, Medical University of South Carolina, Charleston, SC, United States, [2]Ralph H. Johnson Veterans Affairs Medical Center, Charleston, SC, United States, [3]Department of Otolaryngology-Head and Neck Surgery, Medical University of South Carolina, Charleston, SC, United States

Extensive overlapping neural circuits critical to both olfactory and cognitive processing has prompted growing interest in the relationship between olfaction and cognition, including whether olfactory function can serve as an early screening tool for cognitive impairment. Comorbidity of persistent olfactory dysfunction and “brain fog”, often reported in Long COVID, lends additional support for this notion. It remains unknown if post-COVID chronic olfactory dysfunction relates to cognitive impairment, and if specific olfactory and cognitive deficits associate with one another. We examined these questions utilizing baseline data collected from adults (N=40) participating in a treatment study for COVID-related persistent smell loss, called “Study of Chemosensory Enhancement through Neuromodulation Training (SCENT)”. Sniffin’ Sticks assessed odor threshold, discrimination, and identification, while the Montreal Cognitive Assessment (MoCA), Sustained Attention to Response Task (SART), and NIH Toolbox (NIH-TB) Cognition Battery assessed global cognition, sustained attention, inhibitory control, working memory, and cognitive flexibility and speed. Deficits in odor threshold related to more errors of omission (r=-.360, p=.023) and commission (r=-.329, p=.038) on the SART. Deficits in odor discrimination related to deficits in working memory on the NIH-TB picture sequence task (r=.350, p=.027) and lower MoCA global cognition scores (r=.508, p=.001). Deficits in odor identification and working memory (i.e. NIH-TB list sorting) were also related (r=.396, p=.011). The current results indicate associated COVID-related deficits in olfaction and cognition. Future analyses will determine if successful treatment of COVID-related chronic olfactory dysfunction results in improved cognitive function.

209 **Molecular Mechanisms Of Olfactory Training In Dysosmic And Normosmic Individuals**

Ronja Hopf[1], Emely Kruschwitz[2], Thomas Hummel[2], Dietmar Krautwurst[1]

[1]Leibniz-Institute for Food Systems Biology at the Technical University of Munich, Freising, Germany, [2]Department of Otorhinolaryngology, Faculty of Medicine Carl Gustav Carus, Smell & Taste Clinic, Technische Universität Dresden, Dresden, Germany

Olfactory dysfunction can be found in about one-fifth of the population (I. Croy et al., Chem Senses, 2014). Olfactory training with four selected odorants has emerged as a common and effective treatment for these disorders (M. Pieniak et al., Neurosci Biobehav Rev, 2022). A positive training effect on the sensory abilities of patients experiencing general anosmia or hyposmia was not improved using more than four odorants (N. Power Guerra et al., Eur Arch Otorhinolaryngol, 2024). The underlying molecular mechanisms, however, remain unclear. Here we show that positive sensory effects of a typical four-item olfactory training with dysosmic and normosmic individuals is paralleled by a highly significant increase (n=23, $p<0.001$, Wilcoxon signed-rank test) in their olfactory epithelium transcript levels (Rt-ddPCR) of broadly tuned odorant receptor OR2W1, which is known to respond to all four training odorants (F. Haag et al., Food Chem, 2022). No such effect was observed with an increased number of training odorants. These findings suggest a link between olfactory training and changes in odorant receptor transcript levels. Future work will explore potential allosteric interactions between training substances at the receptor level.

211 **Normosomic Patients In A Smell And Taste Clinic**

Antje Welge-Lüssen [1], Thomas Hummel[2]

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Objective: Not all patients presenting themselves to specialized Smell and Taste Clinics exhibit olfactory loss. We aimed to investigate the characteristics of normosmic subjects seeking medical advice for olfactory dysfunction. Methods: Data from 2321 patients seeking advice in the last ten years (Jan 2015 to December 2024) were analyzed. Subjective impairment was evaluated in all using a visual analogue scale. Endonasal endoscopy and olfactory testing (lateralized Sniffin´ Sticks test, composite TDI (threshold, discrimination and identification) score) was performed, diagnosis was made accordingly. Results: In 318 (14%) examinations out of 2321 normosmia was seen, 33 patients (pat.) were examined twice and 6 three times. Data from 273 pat. were analyzed. Main complaint in 74 (27%) pat. (46 female [F], 28 male [M], age [mean, years(y)]: 49 ± 14) was dysgeusia, 47 (63.5%) out of these had bilateral and 27 (36.5%) unilateral normosmia (best TDI, mean: 33.34 ± 2.93), 74 pat. (52 F, 22 M, age: 43 ± 12 y) were suffering from a postinfectious disorder, 47 (63.5%) with unilateral and 27 (36.5%) with bilateral normosmia, mean best TDI: 32.70 ± 2.21). In 19 posttraumatic pat. (7 F, 12 M, age 43 ± 16 y) bilateral normosmia was found in 3 cases only. In 106 (39%) pat. (56 F, 50 M, age 48 ± 14 y) no obvious reason for subjective complaints could be identified, however, in 67 (63%) unilateral hyposmia or anosmia was detected. Subjective impairment was highest in this group. Conclusion: Even though self assessment seems unreliable, 2/3 of patients complaining about an olfactory disorder without obvious reasons exhibited unilateral reduction in function. This suggests that the complaints have to be taken seriously. The current findings are in favor of meticulous testing in this specific group of patients.

213 **Deficits In Olfactory Behaviors In Mice After Subchronic E-Cigarette Exposure**

Sean O'Sullivan[1], Janae Gordon[1], Saheedat Odetayo[1], Kafui Ameko[1], Mufaro Chiduza[1], Agnes Koodaly[1], Ashkon Hazrati[1], Michael Ack[1], Virginia Murray[1], Leyla Aydin[1,2], Tatsuya Ogura[1], Weihong Lin[1]

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Electronic cigarettes (e-cigarettes) are used daily by millions of people worldwide. However, e-cigarette vapor contains various volatile organic compounds, such as formaldehyde, and heavy metals. Previously published studies established a relationship between environmental exposure to these toxicants and olfactory dysfunction. However, the synergistic effects of vaping these compounds and olfactory-guided behavioral impairment has not been investigated. This project aims to investigate the effect of e-cigarette vapor components on the olfactory system. A cohort of mice were split into three treatment groups and one control group: propylene glycol/vegetable glycerin (PG/VG) only, PG/VG + flavorants, PG/VG + flavorants + heavy metals, and air exposure. Groups were exposed twice daily for 8 weeks to simulate subchronic e-cigarette use. Olfactory-guided behavioral assays were performed before and after the exposure to determine potential behavioral effects. We employed a buried food test and a urine/water preference T-Maze to explore if vaping disrupts foraging and odor-guided discrimination. Videos from each group were recorded and analyzed using tracking software from Bonsai. Our findings show that e-cigarette exposure increases the latency to discover buried food, with worse performance in our PG/VG + flavorants and the PG/VG + flavorants + heavy metals groups. We observed lowered preference for a known attractive odor (urine of the opposite sex) in the PG/VG + flavorant + heavy metals group as indicated by decreased time spent with urine compared to the water control. The results suggest that repeated exposure to the flavorants and heavy metals found in e-cigarette vapors may lead to impaired olfactory detection and discrimination, and may precede further vaping induced olfactory dysfunction.

215 **Probing Olfactory Function With The Aromha Brain Health Test And The Brief Smell Identification Test (B-Sit)**

Benoit Jobin[1,2], Hengbin Zhang[1], Beyzanur Ergun[1], Colin Magdama[1,3], Sean Reineke[4], Alefiya Dhilla Albers[1,5], Mark W Albers[1,3]

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We recently developed and validated the digital remote AROMHA Brain Health Test (ABHT), an at-home olfactory battery that can be self-administered in English and Spanish. Previous results showed that the battery distinguishes older adults with amnestic Mild Cognitive Impairment from those with normal cognition (CN), suggesting its utility as a screening tool for development of memory decline due to Alzheimer's disease (AD). Here, we compared the ABHT to the Brief Smell Identification Test (B-SIT), a 12-item scratch-sniff smell identification test used extensively to measure olfactory function. While the B-SIT measures smell identification, the ABHT measures different components of the olfactory function, including odor percept identification (OPID9, OPID9NoGuess, OPID18, OPID18NoGuess), odor discrimination (OD10), percepts of odor episodic memory (POEM), perceived intensity, and identification-confidence. Both tests were administered in sequence to 23 CN older adults (mean age: 66, SD:8.31). We performed correlational and linear regression analyses to analyze the relationship between B-SIT scores and components of the ABHT battery. All identification outcomes of the ABHT correlated with the B-SIT score (OPID9: r=.44, p=.03; OPID9NoGuess: r=.43, p=.04; OPID18: r=.44, p=.03; OPID18NoGuess: r=.55, p=.006). As expected, discrimination (OD10: r=.37, p=.08), memory (POEM: r=.17, p=.42), intensity (r=-.06, p=.78), and confidence (r=.20, p=.36) did not correlate with the B-SIT. Age and sex did not moderate these associations (p>.05). The ABHT's odor percept identification subtests correlated with the B-SIT. These findings support the validity of the ABHT as a comprehensive tool for assessing olfactory function, with potential utility for early detection of risk of developing symptoms of AD neuropathology.

217 **Color-Modulated Olfactory Testing: An Innovative Tool For Early Detection Of Cognitive Decline**

Sally Arnhardt[1], Kristin Steinebach[1], Romy Fuchs[1], Tim Diener[1], Johannes Kornhuber[1], Jessica Freiherr[1,2]

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Dementia and related disorders are an increasing concern, with olfactory loss often being an early indicator. Since odors are regularly perceived in combination with visual stimuli, the aim of this study was to develop a sensitive color-modulated olfactory test as a potential early screening tool for cognitive impairments. Two test versions were developed to assess odor identification under varying conditions. In version 1, response options were presented in colors associated with the target odor, hypothesized to facilitate correct identification. In contrast, version 2 employed colors of one of the distractor items, aiming to increase identification difficulty. Participants aged 50 years and older (n = 44), a group more vulnerable to developing cognitive impairments, performed significantly worse in version 2 compared to version 1, whereas the cohort under 50 years (n = 81) of age showed a reversed trend. Participants with a mild cognitive impairment (MCI, n = 27), categorized using the standardized MoCA test, performed worse compared to the healthy control group, particularly in version 2. Our findings highlight the applicability of the novel olfactory test in clinical and research contexts for cognitive and sensory evaluations, showing that associated colors influence odor identification in heterogeneous groups and may serve as a screening tool for neurodegenerative impairments.

219 **Unique Features Of Nasal Airway And Airflow Improvements Post-Dupilumab: A Computational Investigation Of Its Effectiveness In Relieving Olfactory Losses**

Nidhi Jha, Ahmad Odeh, Zhenxing Wu, Aspen R. Schneller, James Mihalich, Christopher Brooks, Casey Curtis, Monika Craft, Kara Wada, Bradley A. Otto, Kathleen M. Kelly, Kai Zhao

The Ohio State University College of Medicine, Columbus, OH, United States

Dupilumab is a monoclonal IgG4 antibody for treatment of chronic rhinosinusitis with nasal polyps. It has been shown to produce rapid and sustained improvement in olfactory functions even prior to significant reduction of polyps. We used patient-specific computational fluid dynamics modeling to investigate its precise effect on nasal airway patency and airflow patterns to see how these changes may contribute to olfactory improvement. 12 patients completed the Sinonasal Outcomes (SNOT-22), as well as clinical and research CT scans, pre and 3 months post Dupilumab treatment. During the treatment, all patients received a standard 300 mg dupilumab subcutaneously every 2 weeks. Indeed, SNOT22 symptom scores, including an inquiry about smell and taste symptoms, significantly improved from baseline to post-dupilumab (0-5 scale: 4.58 ± 0.51 to 1.25±1.36, $p<0.01$). Nasal airway cross-sectional area (CSA) and airflow rate (AFR) in the middle and superior but not inferior meatuses significantly increased post-treatment (CSA: 0.26±0.19 to 0.59±0.59 cm2, $p<0.05$; AFR: 15.4 ± 20 to 55 ± 50 ml/s, $p<0.05$). These regional increases significantly correlated with olfactory symptoms score (CSA: r=-0.49, AFR: r=0.49-0.50, all $p<0.05$). Surprisingly, nasal resistance did not significantly decrease post-treatment ($p=0.08$). Lund Mackay score significantly improved post-dupilumab (14.4±6.3 to 9.8±4.6; $p<0.05$) and significantly correlated with SNOT-22 scores ($r=0.41$, $p<0.05$), but still with moderate residual polyps. The impact of dupilumab on nasal airway patency and airflow is not uniform but more pronounced in the middle and superior meatus. These unique regional changes may explain previously reported rapid and sustained improvement in sense of smell post- dupilumab.

221 **Chronic Olfactory Inflammation: Its Impact On The Olfactory Epithelium, Olfactory Bulb And Brain Cognitive Function**

Derek Cox, Morning Dove Rose, Kaitlyn Taylor-Cox, Diego Rodriguez-Gil, Russell Brown, Cuihong Jia
Department of Biomedical Sciences, Quillen College of Medicine, East Tennessee State University , Johnson City, TN, United States

Olfactory deficits positively correlate to cognitive dysfunction and are proposed as an early predictor for neurodegenerative diseases. Chronic olfactory inflammation following viral nose infection, including COVID-19, leads to loss of the sense of smell. Whether chronic olfactory inflammation impairs brain function, such as COVID-related cognition and memory decline, is not fully understood. Using an inducible olfactory inflammation (IOI) mouse model that induces TNFα expression under Cyp2g1, a marker for the olfactory epithelium (OE), we investigated the effect of chronic olfactory inflammation on OE, olfactory bulb (OB) and brain cognitive function. Six weeks after induction of TNFα, a massive inflammatory response was observed in the OE, including upregulation of IL-1β, IFNγ, IL-6, and CCL2. Olfactory sensory neurons were lost in a patchy pattern that matches the differential expression of Cyp2g1 in the OE. Basal stem cell proliferation was absent in injured and intact regions. Smell function, measured by buried food and olfactory habituation/dishabituation tests, was also impaired. In the OB, IOI elevated IL-1β and IL-6 mRNA, activated microglia and enhanced leukocyte infiltration. These data indicate that chronic OE inflammation disrupts the OE and its regenerative capacity, which then causes an inflammatory pathology in the OB. Importantly, hippocampus-mediated learning and memory, tested by Barnes maze and novel object recognition, was also compromised in the IOI mice. The IOI-induced hippocampal pathology is under investigation. Together, this study reveals an OE-OB-hippocampal pathway that might be correlated to cognitive decline following COVID-19-induced chronic olfactory inflammation.

223 **Life Satisfaction In Cancer Patients With And Without Chemosensory Dysfunction**

Victoria Esparza[1], Vicente Ramirez [1], Alissa Nolden[2], Kara Stromberg [3], Valentina Parma [1]
[1]Monell Chemical Senses Center, Philadelphia , PA, United States, [2]University of Massachusetts Amherst , Amherst , MA, United States, [3]Fox Chase Cancer Center , Philadelphia , PA, United States

Chemosensory dysfunctions (CD) are symptoms often experienced by cancer patients. Albeit common, these symptoms lack guidelines for management and are rarely addressed by healthcare providers, and therefore, how taste and smell dysfunctions affect quality of life in cancer patients is understudied. To address this gap, we analyzed data from the 2021 National Health Interview Survey (NHIS). The sample included 3,654 subjects (mean±SD: 68±13 years, range:18-99 years; 58% F; 85% non-hispanic white) who self-reported having cancer and self-assessed whether they had difficulty tasting, difficulty smelling, and reported life satisfaction (binary) in the last 12 months. 20.3% reported smell dysfunction (n=741; 70±12 years; 49% F) and 11.9% reported taste dysfunction (n=435; 70±12 years; 52% F), and 9% reported both smell and taste dysfunction (n=330; 71±12 years; 51% F). After adjusting for age and sex, a logistic regression revealed that cancer patients reporting difficulty tasting had 64% decreased odds of reporting life satisfaction compared to those who did not report difficulty tasting ($z=-6.3$, $p<0.0001$, CI[.27,.50]). Similarly, cancer patients reporting difficulty smelling had 43% decreased odds of reporting life satisfaction compared to those who did not report trouble smelling ($z=-3.7$, $p<0.0001$, CI[.43,.77]). Considering that the prevalence of CD is often underestimated when measured with self-reports, we consider this a conservative scenario to test the hypothesis that CD is associated with decreased life satisfaction in cancer. These findings call for a serious assessment of CD in cancer patients to improve quality of life.

225 **Objective Assessment Of Long-Term Impact Of Covid-19 On Multiple Sensory Functions: A Preliminary Report**

Veronica L. Formanek[1], Ahmad Odeh[1], Christina Smith[1], Nidhi Jha[1], Junichi Tajino[1], Jessica H. Lewis[1], Lauren Gastineau[1], Shivani Patel[1], Songzhu Zhao[2], Lai Wei[2], Aaron C. Moberly[3], Daniel M. Merfeld[1], Christopher T. Simons[4], Megan J. Kobel[5], Kai Zhao[1]

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This study investigates post-acute sequelae of SARS-CoV-2 infection (PASC) on broad sensory functions. 60 subjects (age 27-78) contracted COVID-19 between 1/17/2020-12/21/2023 and continue to have symptoms (4.3-52.9, median=27.48 months) were recruited. Objective testing included 1) smell: 9-Item NIH Toolbox odor identification, detection threshold to phenyl-ethyl alcohol, and retro-nasal candy test; 2) taste: modified NIH toolbox; 3) chemesthesis: menthol lateralization thresholds; 4) hearing: pure-tone audiometry, otoacoustic emissions, speech-in-noise recognition, and Dichotic Digits Test; 5) vestibular: video head impulse testing, Subjective Visual Vertical, vestibular perceptual thresholds, and modified Romberg balance test. Overall, subjects self-reported high overlapping sensory losses: 67.3% smell, 63.6% taste, 56.5% balance and dizziness, 31.8% auditory, and 51.3% brain fog or cognitive dysfunctions, with varying discrepancy to the objective losses (smell 65.5%, taste 16%, vestibular 31.6%, hearing 53.4%, and cognition 19.1%). Significant differences were found between subjects reporting diminished vs distorted senses, and between sensory stimuli (e.g. sweet vs sour). Significant associations were found between objective vestibular and auditory losses ($p=0.04$), cognitive and vestibular impairments ($p=0.0207$), nasal trigeminal and self-reported smell/taste losses (23/30), but not between objective smell and taste dysfunctions. Hospitalization significantly associated with smell, cognitive, and vestibular dysfunctions ($p<0.05$). Age significantly associated with auditory and vestibular dysfunctions ($p<0.01$). COVID-19 impacts sensory systems broadly and differently, driven in part by aging and initial disease severity. Subjective symptoms were not always corroborated by objective deficits.

227 **Extracting Smell Disorders As Early Indicators Of Neurodegenerative Diseases Using Natural Language Processing**

Evan Guerra, Halil Kilicoglu
University of Illinois Urbana-Champaign, Champaign, IL, United States

Smell loss is an important early symptom of neurodegenerative diseases (NDs) and varies across conditions, offering potential as an early indicator of disease progression. Despite ~1,800 PubMed articles on NDs and olfaction, natural language processing (NLP) tools are underutilized for extracting and analyzing ND-olfactory relationships from vast scientific literature. By utilizing NLP methods, we extract olfactory information such as perceived intensity, detection threshold, and identification, analyze diagnosed smell disorders, and assess current NLP limitations in this domain. Using PubMed abstracts on five NDs (Alzheimer's, Parkinson's, multiple sclerosis, dementia, progressive supranuclear palsy), we annotated 497 abstracts for five entities: olfactory dysfunction, disease, smell test, odorant, and perceiver, as well as relationships (positive correlation, negative correlation, and association). Our NLP system utilized PubMedBERT and achieved an F1 score of 0.86, Precision of 0.91, and Recall of 0.81 on extracting olfactory-disease relationships. Alzheimer's was the most mentioned ND, with anosmia as the most frequent olfactory entity. Strong connections were identified between anosmia and dementia, while Alzheimer's and Parkinson's were linked to broader terms like "olfactory dysfunction." These findings reveal gaps in current knowledge sources for olfactory terms and highlight the promise of NLP in advancing understanding of smell-related ND research. More targeted NLP efforts are needed to overcome limitations and deepen insights into ND-olfaction relationships.

229 **Examining The Effects Of Air Pollution On Odor Identification In Aging**

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Prior analysis of the 1986 National Geographic Smell Survey (NGSS) linked air pollution exposure to impaired olfactory function, with a 5-12% reduction in the odds of correctly identifying odors per standard increase in gaseous air pollutants. Yet, results were mixed: pollutants like O_3 were significantly associated with low odor identification scores (<2 odors identified) but not high scores (4 vs. 5 odors). We hypothesize that air pollution disproportionately affects individuals at greater risk for reduced olfactory function, such as older adults. This study investigates age-stratified effects of air pollution on olfactory function. NGSS data were merged with EPA Air Quality System data. Exposures to PM_{10}, SO_2, O_3, NO_2, and Pb were assigned by zip code. Age groups (10-20, 21-35, 36-50, 51-65, 66-80, 80+ years) were analyzed using multilevel binomial logistic regression with random intercepts. Covariates included sex and smoking status. Multipollutant models revealed significant associations between pollutant exposure and odor identification scores for NO_2 and O_3 across most age groups, except for individuals 80+ (N=588). NO_2 exposure was negatively associated with olfactory performance in all age groups, strongest in ages 36-50 (OR=0.93, CI 0.91-0.94) and weakest in ages 10-20 (OR=0.97, CI 0.94-0.996). O_3 exhibited a positive association with odor identification in individuals aged 20-80 (OR=1.04-1.06). NO_2 is significantly associated with impaired olfactory function across most age groups, except the oldest cohort, highlighting its widespread impact. The association with O_3 may indicate a protective effect; however, the inverse relationship between O_3 and NO_2 suggests potential confounding by local environmental conditions, which deserves to be further investigated.

231 **Pre-Infection Covid-19 Vaccination Protects Against Smell Loss**

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Objectives: Smell loss (anosmia) is a common and distressing symptom of COVID-19, with potential long-term consequences on quality of life. This study evaluates the protective effect of COVID-19 vaccination on olfactory and gustatory function using the University of Pennsylvania Smell Identification Test (UPSIT) and the Waterless Empirical Taste Test (WETT). Methods: A total of 250 individuals were assessed, including 128 who were vaccinated prior to contracting COVID-19 and 122 who were unvaccinated at the time of infection. UPSIT and WETT scores were compared between the two groups using one-way ANOVA. A subgroup analysis was performed for individuals under 70 years of age to evaluate potential age-related differences in the protective effects of vaccination. Results: Vaccinated individuals exhibited a higher mean UPSIT score (34.37) compared to the unvaccinated group (32.58), with results nearing statistical significance ($p = 0.0539$). However, among participants younger than 70 years, vaccinated individuals had significantly higher UPSIT scores (35.41) compared to their unvaccinated counterparts (32.95), with a statistically significant difference ($p = 0.0064$). WETT scores showed no significant difference between vaccinated (35.08) and unvaccinated (34.34) individuals ($p = 0.5095$). Conclusions: COVID-19 vaccination appears to provide a protective effect against long-term smell loss, particularly in younger individuals. Vaccinated individuals demonstrate better preservation of olfactory function, as indicated by higher UPSIT scores. These findings underscore the potential role of vaccination in mitigating the sensory deficits associated with COVID-19 and highlight the need for further research to explore the underlying mechanisms of this protection.

233 **High Pesticide Exposure Events And Olfactory Impairment Among U.S. Farmers**

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Background: Environmental exposures, such as pesticides, may contribute to olfactory impairment (OI) in older adults, but empirical evidence is limited. Objectives: To examine the association between high pesticide exposure events (HPEEs – e.g., major accidental spills) and OI in the Pesticide and Sense of Smell Study (PASS), a sub-cohort of the Agricultural Health Study (AHS).
Methods: PASS included 2,545 predominantly white male farmers (aged 70.3±9.6), sampled from the AHS Phase 4 follow-up (2013-2015), who completed the 12-item Brief Smell Identification Test (B-SIT) in 2020–2021. We defined OI as a B-SIT score ≤8. Farmers also self-reported their olfaction status before the test and answered questions about their experience completing the B-SIT. HPEEs were reported both in PASS and prior AHS surveys. We used a doubly robust inverse probability of censoring weighted target maximum likelihood estimation to assess associations between HPEEs and OI-related outcomes, accounting for sampling design, missingness data, and potential confounders. Results: Using the HPEE reported in PASS as an example, compared to those who never had a HPEEs, farmers with a history of HPEEs had a 30% higher risk of self-reported OI (relative risk/RR = 1.30, 95% CI: 1.04, 1.62). However, HPEEs were not associated with B-SIT-tested OI (RR = 0.97, 95% CI: 0.83, 1.15) or perceived testing experience, including reporting substantial difficulty in identifying B-SIT odors (RR = 0.94, 95% CI: 0.78, 1.13) and reporting them as very weak (RR = 1.01, 95% CI: 0.78, 1.30). Similar results were obtained in the analyses using HPEE data from previous AHS surveys.
Conclusions: HPEEs were associated with subjective complaint of olfactory loss but not with objectively-tested olfaction among farmers, which warrants further investigation.

235 **Sensory Sensitivities In Autism Spectrum Disorder: Insights From The Glasgow Sensory Questionnaire**

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Sensory sensitivities are a hallmark feature of Autism Spectrum Disorder (ASD) and can significantly impact daily life[1]. However, research on sensory experiences in ASD remains limited, particularly in comparing chemosensation in adults with and without ASD. In this study, we assessed sensory hypersensitivity and hyposensitivity using the Glasgow Sensory Questionnaire (GSQ), a 42-item self-reported measure specifically developed for adults with ASD[2]. The GSQ evaluates sensory experiences across seven domains (i.e., visual, auditory, tactile, proprioception, vestibular, olfactory and gustatory), investigated with 6 questions each. The total score ranges from 0 to 168, with higher scores indicating higher sensitivity (both hypo and hyper). We tested 72 participants out of the 268 participants from the University of Pennsylvania Autism Spectrum Program of Excellence (ASPE) cohort, including 38 adults with ASD (age: 33±10 years, 92% female) and 34 non-ASD controls (age: 33±10 years, 85% female). The comparison of the total GSQ score across groups reveals that participants with ASD report significantly more hypo and hypersensitivities as compared to non-ASD participants (ASD: 74±28 points, non-ASD: 24±14 points, U = 1149, p = 1.84e-10). Smell [ASD: 8 ± 4 points, non-ASD: 3±2 points, U = 1149, p = 1.84e-10] and taste [ASD: 10±5 points, NT: 3±2 points, U = 1114, p = 1.21e-7] GSQ scores are comparable to each other. Findings on chemosensory sensitivities are comparable to all other senses, except for audition, for which the sensitivity is greater in both ASD and non-ASD participants (p_s <0.001). Our findings provide valuable insights into sensory processing differences in ASD as compared to non-ASD individuals, with implications for understanding chemosensory sensitivities in adults with ASD.

237 **Limited Effects Of Isolated Congenital Anosmia On Cerebral White Matter Morphology**

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Individuals with congenital sensory loss experience a persistent absence of input from the affected sense throughout their development. For our non-chemical senses, this lack of sensory input has been associated with alterations in brain morphology, mainly in or near cerebral regions normally devoted to processing of the missing sense. In contrast, we have in multiple studies demonstrated that the only consistent morphological finding within the grey matter of individuals born without the sense of smell (isolated congenital anosmia; ICA), are changes in or near the olfactory sulcus, associated with small or absent olfactory bulbs. For the connecting tissue of the brain, the white matter (WM), previous studies have yielded inconsistent findings. Here, we aimed to establish whether individuals with congenital anosmia exhibit alterations in WM by comparing WM volume between 49 individuals with ICA and 49 age- and sex-matched controls. Consistent evidence from both voxel-based morphometry and multi-voxel pattern analysis demonstrates that individuals with ICA show decreased WM in areas surrounding the olfactory sulcus. Importantly, no WM alterations were found in areas surrounding the olfactory (piriform) cortex. Contrary to the literature on visual and auditory loss, our findings suggest that, despite lifelong olfactory deprivation, cerebral morphological alterations are limited. The changes observed are primarily localized around the olfactory sulcus and likely attributed to the absence of olfactory bulbs. The possibility of the olfactory cerebral system being occupied by other functions in these individuals, which would limit morphological changes, should be further investigated.

239 **Prognosis Of Chemosensory Recovery Among Long Covid-19 Patients &Ndash; Objective Assessment At 3 And 6 Months Follow-Ups**

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Chemosensory dysfunction is a hallmark symptom of COVID-19 infection, with many patients experiencing symptoms beyond initial infection. This ongoing study aims to capture the timeline in chemosensory recovery following post-acute sequelae of SARS-CoV-2 infection (PASC). This preliminary analysis includes 23 patients (30-74 years old, median: 56) who contracted COVID-19 from 3/2020 to 11/2023, 8-51 months (median: 31) prior to the initial visit. All then completed a 3-month follow-up, and 12 completed a 6-month follow-up. Patients received objective testing of 1) smell function using the 9-Item NIH Toolbox Odor Identification (ID) Test, detection threshold (ODT) to phenyl-ethyl alcohol (PEA), and retro-nasal flavor identification (candy test); 2) taste function using the modified NIH toolbox. Patients self-reported a high prevalence of smell (78%) and taste (65%) losses. 78% confirmed objective smell loss, while only 20% confirmed objective taste loss. At 3-month follow-up, patients exhibited significant improvements in objective smell (Odor ID, p=0.0139) function but not objective taste (NIH Toolbox, p=0.107), yet the number of patients exhibiting objective chemosensory losses remained high (smell 43%, taste 22%). From 3- to 6-month follow-up, patients showed significant decline in objective taste (p=0.0496) function. These findings suggest significant fluctuations in chemosensory function following COVID-19 infection, with prognosis prolonged and uncertain, and self-report being unreliable, especially for taste loss. Future work will continue to evaluate smell and taste for a larger sample size and longer time duration.

241 **Olfactory System Alterations In A Novel Model Of Dopaminergic Loss By 6-Ohda Injections In Adult Zebrafish**

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Parkinson's Disease (PD) is a neurodegenerative disorder marked by dopaminergic neuronal loss and motor impairment. Olfactory loss affects over 95% of PD patients, often preceding motor deficits. However, the mechanisms linking PD to olfactory dysfunction remain unclear. One hypothesis suggests that dopaminergic loss leading to retrograde degeneration in the olfactory system underlies this phenomenon. To study this we use zebrafish, whose olfactory system is analogous, yet simpler, to those of mammals. We developed a model of dopaminergic loss in the OB by injecting 6-hydroxydopamine (6-OHDA) into the cerebrospinal fluid at the ventricular zone between the OBs and telencephalon. We sought to selectively target dopaminergic neurons in the OB without affecting posterior motor nuclei to preserve locomotion. We used immunohistochemistry to evaluate post-injection structural alterations and degeneration, and behavioral assays to assess olfactory function. Results confirmed significant dopaminergic neuronal loss in the OB, accompanied by morphological changes in olfactory glomeruli. We also observed degeneration of olfactory sensory neurons (OSN) in the olfactory epithelium (OE), suggesting retrograde degeneration. Neuroinflammatory responses, marked by increased astrocyte and leukocyte activity, were prominent in both the OB and OE during the first seven days post-injection. These degenerative changes correlated with selective disturbances in olfactory-mediated responses, indicating functional alterations. We also report a proliferative response in the OB and OE suggesting repair mechanisms launched following dopaminergic loss. This novel zebrafish model provides valuable insights into

the relationship between dopaminergic neuronal loss and olfactory dysfunction in PD.

243 **Characterizing Olfactory Brain Responses In Young Infants**

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Odor perception plays a critical role in early human development, but the underlying neural mechanisms are not fully understood. To investigate these, we presented two appetitive and two aversive odors to infants at one month of age while recording functional magnetic resonance imaging (fMRI) and nasal airflow data. To enable MRI scanning at this early age, infants slept during odor presentation. Whole brain analyses revealed that compared to clean air, odors evoke fMRI activity in bilateral olfactory cortex (encompassing piriform cortex and amygdala) as well as thalamus. Analysis of odor-evoked fMRI responses in anatomically defined regions of interest further showed significant responses in piriform cortex, amygdala, olfactory tubercle, and entorhinal cortex, whereas no significant responses were found in anterior olfactory nucleus. Moreover, fMRI response magnitudes in piriform cortex and amygdala differed across odors. However, in contrast with prior work in adults, we did not find evidence that odor stimuli evoke discriminable fMRI activity patterns using two different multivariate pattern analysis techniques. Finally, the average inhale airflow rate was higher for appetitive odors than aversive odors, suggesting that, similar to adults, infants may modulate their respiration to reflect odor valence. Overall, these results show strong neural responses to odors at this early developmental stage and highlight nasal airflow as a behavioral metric for assessing odor preferences in infants.

245 **Premotor Inputs Modulate Preparatory Activity In The Gustatory Cortex**

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Studies have demonstrated multiple roles for the gustatory cortex (GC) in processing cognitive signals related to a gustatory experience. Importantly, GC represents the progression of taste sensory coding into preparatory signals predicting lick decisions in the context of a delayed-response task where taste guides directional licking. While decision-related activity was observed in GC, the neural mechanisms underlying this representation have not been studied. Given the connections between GC and frontal cortices involved in guiding goal-directed actions, external inputs may modulate preparatory activity in GC during the motor planning of lick decisions. A probable candidate in coordinating GC activity in the context of a delayed-response task is the anterior-lateral motor cortex (ALM). This subregion of the mouse frontal cortex is involved in the planning and execution of goal-directed licking. In this study, we investigated the coordination between GC and ALM in a taste-based, directional licking task with a delay period. Simultaneous electrophysiological recordings were performed to compare the temporal coding of task variables between the two regions. Preparatory activity for licking was found to begin earlier in ALM than in GC. Analysis of trial-type selectivity revealed distinct representations in decision-related coding between the two regions. To determine if ALM is a source of preparatory signals to GC, we performed transient optogenetic inhibition of ALM during the delay period while recording GC activity. Inactivation of ALM reduced direction selective preparatory activity in GC, supporting a role for ALM as a source of such signals to GC. Our findings demonstrate that cortical premotor inputs significantly contribute to GC activity during taste-guided decision making.

247 **Modulation Of Unimodal And Multimodal Signals In The Gustatory Cortex By Posterior Piriform Cortex Photosuppression**

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Flavor perception relies on the integration of gustatory and olfactory signals, a process thought to involve interactions between the chemosensory cortices. Recent findings reveal that neurons in the gustatory cortex (GC) represent odor-taste mixtures as distinct from their unimodal components, highlighting its role in processing complex chemosensory stimuli. To investigate how network dynamics influence the representation of intraoral chemosensory stimuli, we virally expressed an inhibitory opsin (AAV-CAMKII-ArchT-GFP) in excitatory neurons of the posterior piriform cortex (pPC), a multisensory region of the olfactory cortex. We recorded activity from 266 GC neurons in six behaving female rats during the intraoral delivery of two odors (isoamyl acetate; ethyl butyrate), two tastes (sucrose; citric acid), and two specific odor-taste mixtures (IAS; EBCA), with and without pPC photosuppression. Our preliminary results show that pPC photosuppression differentially impacts the representation of the two mixtures and their components. Population decoding analyses revealed that pPC photosuppression delayed the onset of classification accuracy for the isoamyl acetate-sucrose mixture and its components (0.25–0.5 seconds), whereas decoding performance for the ethyl butyrate-citric acid mixture and its components was perturbed later (0.5–1 second). A majority of GC chemoresponsive neurons exhibited at least one stimulus response significantly modulated by pPC photosuppression. Future analyses will explore whether distinct subpopulations of GC neurons contribute to the observed temporal and stimulus-specific differences in response representations. These findings suggest how interactions between chemosensory cortices may contribute to the neural representations underlying flavor perception.

249 **Optogenetic Stimulation In The Gustatory Cortex Mimics Taste Input Patterns**

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Flavor perception depends on integration of multiple sensory and extrasensory signals converging on gustatory cortex (GC). Several studies recently provided insight into the rules underlying integration of inputs, but the exact mechanisms remain elusive. Precise control over input characteristics would allow for further characterization of integrative computations and a test of their causal role in producing neural and behavioral responses. Here, we hypothesize that optogenetic stimulation provides a method for controlled manipulation of input strength to GC at the single neuron and population level. To test this, we injected AAV coding for ChR2 in the GC of rats, followed by recording of single-unit spiking activity in the GC of anesthetized animals in response to photo-stimulation. We recorded from 96 units in response to 2.5 s continuous stimulation at two different light strengths. Both light strengths evoked significant responses, sustained over the 2.5 s stimulation period in the majority of recorded units (84% low light, 70.5% high light). Of the responsive units, most were activated by network-level effects, rather than direct photo stimulation (85.7% low light, 66.7% high light). Responses could be excited or inhibited compared to baseline (excited: 67.3% low light, 62.5% high light). Response properties in terms of number of neurons, evoked firing rate, sign and temporal profile were highly similar to a natural taste response. These findings show that optogenetic stimulation in the GC is a reasonable way to mimic input patterns evoked by taste stimuli, opening opportunities to study different aspects of information processing in GC. Ongoing work will probe optogenetic responses in awake animals and quantify the effect on network-level activity through local field potential analysis.

251 **Gustatory-Olfactory Cortical Interactions In Response To Multimodal Stimuli**

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Tastes and smells often appear in tandem, creating the experience of flavor. While there are many components that must be understood together in context to better grasp the cortical processing of flavors, research is beginning to describe how higher-order chemosensory cortical areas process multimodal chemosensory in detail. The higher order cortical areas that process taste, smell, and flavor include gustatory cortex (GC) and piriform cortex (PC). These areas change their activity when a combination of taste and smell are perceived. When recording electrophysiological signals from either area, responses to both taste and smell are observed. A question that remains is how the coherence between GC and PC is modulated when unimodal stimuli or multimodal stimuli are perceived and whether the coherence depends on if smell is delivered retronasally (through the mouth) or orthonasally (into the nares). We demonstrate interactions of this flavor network and changes in its overall coherence with multi-site multi-electrode electrophysiological recordings.

253 **A Comparison Of Cortical Taste Representations Arising From Free Licking And Intraoral Delivery**

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Historically, freely-moving electrophysiology and lickometers have been considered largely incompatible; artifacts introduced by lickometers prevent the tracking required for stimulus control. For ephys experiments, tastes have typically been delivered directly into the mouth of anesthetized animals or via intraoral cannula (IOC) in awake animals, despite the obvious limitations on naturalism involved in both cases. Recent techniques have made strides in reducing abstraction; photobeam lickometers are able to record licking without electrical artifact, and calcium imaging is indifferent to electrical noise, both of which have facilitated the investigation of cortical taste representations in active licking animals. Still, limitations remain–the temporal resolution of Calcium imaging is much lower than electrophysiology, and technical considerations have limited the use of photobeam lickometers to restrained animals, which limits their benefits. Much of this work is premised on the untested assumption that taste responses to licking are incomparable to responses to IOC delivery. In an attempt to reconcile these limitations and investigate the potential effects of route of ingestion on taste representations, we developed a paradigm using both IOC and a photobeam-based brief-access lickometer to deliver tastes to rats implanted with multielectrode arrays. This allows us to record gustatory cortical taste representations in freely moving, freely drinking animals with the full resolution of electrophysiology, and contrast that directly with IOC-evoked taste representations within subjects. With this design, we were able to test our hypothesis that route of administration will alter the taste response to an extent, but that the general structure of taste representations will remain largely the same.

255 **Inhibitory Plasticity Controls Gustatory Cortical Circuit Refinement In The Postnatal Period**

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Sensory cortical circuits undergo refinement during the postnatal period which contributes to complex functions including sensory perception, decision-making, and cognition. During these critical periods, circuit refinement requires synaptic plasticity and maturation of inhibition, and these processes are modulated by sensory experience. For the sensation of taste, our recent studies found that taste experience at weaning influenced sweet preference and cortical inhibition in gustatory cortex (GC), the primary sensory region for taste (Schiff et al, 2023). Here, we delineate the time course of postnatal maturation in GC with a focus on cellular and circuit properties. We used whole-cell patch-clamp electrophysiology, immunohistochemistry, and channelrhodopsin-assisted circuit mapping to track postnatal changes in GC. We recorded from GC pyramidal neurons in young

(P17-24), juvenile (P35), and young adult (P56) male and female mice and observed an increase in inhibitory synaptic transmission (IPSCs) with no observed changes in excitatory synaptic transmission (EPSCs), suggesting a developmental shift in the excitatory-to-inhibitory ratio. The changes in inhibition were accompanied by an increase in parvalbumin fluorescence intensity and accumulation of perineuronal nets on PV-expressing interneurons (PV^+ INs). We also observed circuit reorganization with a reduction in inhibitory connectivity onto pyramidal neurons in adulthood compared to weaning. These results suggest that GC circuit refinement is associated with maturation of inhibition, specifically PV^+ INs. Understanding the sequences of postnatal refinement will allow us to better understand how the interaction of cellular mechanisms, nutrition, and early life sensory experience influences brain development and neurodevelopmental disorders.

257 **Integration Of Appetitive Features In The Orbitofrontal Cortex During Food-Based Choices**

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Decisions about food options require integrating chemosensory features with non-chemosensory features such as food availability, quantity, and effort. The orbitofrontal cortex (OFC) is thought to play a key role in integrating this broad set of features for appetitive decision-making. Numerous studies suggest the OFC encodes the value of chosen outcomes and represents specific features of available options during decision processes. However, it remains unclear how the OFC integrates this information to assign values to offers during decision-making. To investigate this, we recorded activity from 485 neurons in the OFC while rats performed a food-based economic decision-making task. In this task, rats made appetitive decisions by integrating the type and amount of food to select their preferred offer. Across ~300 trials per session, rats exhibited consistent choice behavior, allowing for precise estimation of food preferences during the session. Our results show that features such as food type, food amount, offer location, choice location, and offer value are represented during the offer presentation phase, with value representations strengthening as the decision point approaches. Supporting the hypothesis that the OFC integrates these features to evaluate offers, we observed that the dimensionality of ensemble activity peaked during the offer presentation phase and decreased as the decision point neared.

259 **Investigating Intra-State Dynamics In Taste-Evoked Gustatory Cortex Responses In Rats**

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Cortical taste-processing is comprised of a sequence of discrete states of neural activity (Mahmood et al., 2023). State changes, detected using Hidden Markov Modelling (HMM), have been observed in stimulus-evoked neural population activity in both the Gustatory Cortex and Basolateral Amygdala. While previous work has shown that constant-emission HMMs (i.e., models that treat activity within a single state as a fixed pattern plus noise) describe neural population activity better than either trial-averaged PSTHs or Drift-Diffusion models, the assumption of perfectly stationary activity is simplistic (Sadacca et al., 2016; Mahmood et al., 2023). Indeed, previous analyses show that both onset-time and duration of states vary from trial-to-trial. We hypothesize that this variability is governed by hitherto overlooked intra-state dynamics—that differences in the speed with which within-state dynamics reach "completion" may determine differences in state duration. To interrogate this question directly, I have employed a variety of computational methods for quantifying ensemble behavior to better investigate intra-state dynamics in taste-evoked population activity. Our analyses show that intra-state dynamics within cortical activity across a battery of taste stimuli are aligned to state-transitions inferred using constant-emission HMMs, and are demonstrably different from noise (as expected by a constant-emission model). Ongoing work is investigating an explicit link between these intra-state dynamics and duration of taste-processing states. The characterization of these intra-state dynamics will allow for greater insight into the mechanistic models underlying these highly non-linear dynamics and provide additional constrains for theoretical models generating such dynamics.

261 **Olfactory Modulation Of The Medial Prefrontal Cortex Circuitry: Contribution To Social Behavior In Mice**

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Social motivation and social recognition are key elements of social cognition, which is crucial for the formation of a structured society. Impairments in social cognition are observed across a range of neurological and neuropsychiatric disorders. The anterior olfactory nucleus (AON), a cortical region that receives direct inputs from the olfactory bulb, is a critical hub for social memory in mice. However, the neurocircuitry underlying the AON function in social behavior is not fully understood. Here using CRISPR-CAS9 gene editing technique, we generated a mouse line which allows genetic access to AON neurons and examined their whole-brain projection. We found that AON neurons directly project to the medial prefrontal cortex (mPFC), a region that exerts top-down control of social behavior. AON neurons make monosynaptic excitatory inputs onto pyramidal neurons in

all layers of mPFC. We further demonstrated that the AON neurons and their axons in the mPFC are active during various behaviors including social investigation. Finally, chemogenetic inhibition of the AON-mPFC pathway impairs social behaviors in mice. Taken together, this study reveals an olfactory-prefrontal circuit that contributes to social cognition in mice.

263 **Anatomical And Physiological Charaterization Of Long Range Pathways From Hippocampus To Anterior Olfactory Nucleus**

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The physiological and pathophysiological roles of the anterior olfactory nucleus (AON) have drawn increasing recognition due to its pivotal position in the olfactory system, receiving input from the olfactory bulb and sending output to several downstream structures. Additionally, AON is subject to significant top-down modulation from multiple cortical and subcortical brain regions, including the hippocapmpus (HPC). Recent studies have identified two major topographic HPC to AON pathways: intermediate HPC to the dorsal/lateral AON (iHPC-AOD/AOL) and ventral HPC to the medial AON (vHPC-AOM), both of which are crucial in encoding odor-based episodic memory. However, the physiological mechanisms driving top-down modulation of signal processing via these long-range pathways at the cellular and synaptic levels remain elusive. In this study, we addressed this question in mice by combining retrograde and anterograde tracing, whole brain clearing, optogenetics, in vivo and in vitro electrophysiology, leading to the following major findings: (1) HPC-AON projections were visualized in three dimensions within the whole-brain context; (2) spiking activities were evoked by optogenetic stimulation of HPC projections in the AON; (3) glutamate-mediated excitatory responses were observed in both pyramidal cells and interneurons upon stimulation of HPC projections. Although these results align with previous studies, our study provides the first electrophysiological evidence for the HPC-AON projections. Moving forward, further investigations will aim to characterize the pathway- and cell-type-specific synaptic transmission in the AON with the ultimate goal of advancing our mechanistic understanding of the functional significance of this particular top-down modulation.

265 **Human Olfactory Organoids As An *In Vitro* Model Of The Olfactory Epithelium**

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The olfactory epithelium (OE) is a distinctive neuroepithelium capable of regeneration throughout life. However, injuries can lead to olfactory dysfunction, significantly affecting safety, nutrition, and quality of life. Direct studies of OE biology in humans have been limited due to restricted access to human tissue and lack of a human-based model system. We have successfully obtained human superior turbinate biopsies from adult and pediatric subjects, with tissue positive for olfactory cell markers on immunofluorescence, indicating the presence of OE. When cultured in media supplemented with niche factors, dissociated cells generate olfactory organoids. We performed immunostaining of the organoids using antibodies against OE markers, such as NCAM (immature and mature olfactory sensory neurons (OSNs)), olfactory marker protein (OMP; mature OSNs), SOX2 (globose basal cells (GBCs) and sustentacular cells (SCs)), keratin-5 (K5) (horizontal basal cells (HBCs)), and keratin-8 (K8) (SCs). Results demonstrate the presence of OE cell-type markers: NCAM+ cells have neuron-like morphology with a long process and a dendritic knob, cell body, and long axon, typical components of an OSN. We then performed RT-qPCR to quantify gene expression of OE cell types, demonstrating expression of markers for mature OSNs (OMP), SCs (SOX2, EZRIN), GBCs (SOX2), and HBCs (KRT5, SOX2). Organoids show Ca^{2+} release in response to odorant exposure, a surrogate for function. As a control, organoids cultured from inferior turbinate (non-OE) tissue do not mobilize Ca^{2+}. This suggests organoids contain functional OSNs, further supporting the model. In summary, preliminary data supports a novel human olfactory organoid model which may help investigate OE biology in normal and diseased states, with potential for therapeutic insights.

267 **Assessing Retronasal Smell Perception In Young Children Using A Pictorial Rating Scale And Facial Action Coding**

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Flavor perception is a critical determinant of food choice, which directly relates to risk for disease. Previous work has shown that early childhood marks a critical time for establishing flavor preferences. Often referred to simply as “taste”, flavor is in fact a multisensory experience that combines taste and retronasal olfaction. Although taste preferences are innate, the development of retronasal odor preferences remains unknown, partly due to the difficulty in assessing flavor perception in young children. The primary goal of this study is assess differences in retronasal odor perception between young children and adults using a pictorial rating scale and facial expressions. Children ages 3 to 6 years old (n=88) and one of their parents (n=88) were asked to sample solutions containing either a taste or odor. A three step protocol was implemented to assess detection and hedonic evaluation using a pictorial rating scale. Detectability and hedonic ratings for sweet and bitter tastes followed predictable patterns in both age groups, demonstrating validity of the rating scale. With respect to odor perception, detectability of odors was lower among children. Compared to adults, some odors (mango and apple)

were rated as negative more frequently by children, whereas other odors (broccoli and pumpkin) were rated as positive more frequently by children. Facial action units (AUs) were scored by a FACS-certified coder for a semi-overlapping dataset of child-parent dyads (n= 123 dyads). Following a similar pattern to the rating data, broccoli and pumpkin odors elicited fewer negative AUs, while apple and mango elicited more negative AUs among children compared to adults. Together, this suggests that retronasal odor preferences are not innate and can potentially be modified by experience.

269 **Essential Roles Of Hedgehog Antagonist *Hhip* In Filiform Papillae Development**

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Hedgehog (HH) signaling is crucial for embryonic tissue development, including the tongue. The HH pathway antagonist, Hedgehog-interacting protein (HHIP), modulates the HH ligand gradient to ensure precise spatial and temporal pathway activation. While HH gradient influences taste fungiform papilla (FP) and non-taste filiform papilla (FILIFP), a HHIP-specific role remains unexplored. In adult mice, we showed HHIP expression in FILIFP but not in FP. Ectopic HHIP expression in FP alters taste organ maintenance and regeneration. Recently, we observed *Hhip* gene expression in early postnatal FILIFP and lingual stromal cells, including a few within the connective tissue core of FP. Yet, its biological relevance in tongue tissues remains unclear. We used X-gal staining of $Hhip^{lacZ}$ mouse tongues and HHIP antibody immunostaining to map *Hhip* expression in embryonic tongue and $Hhip^{lacZ/lacZ}$ (mutant) to assess *Hhip* function at embryonic day 18.5. We observed *Hhip* expression in suprabasal FILIFP epithelium, the connective tissue core of both FP and FILIFP, and the lamina propria. There were no apparent changes in FP morphology and count, vimentin+ stromal cells, and tongue proliferation and innervation, but collagen expression was disrupted in the mutant. Strikingly, *Hhip* deletion led to dysmorphic FILIFP, impaired differentiation, and ectopic proliferation in FILIFP epithelium suprabasal layers. Further, HH-responding *Gli1+* cells in the lingual epithelium were elevated in the mutant. These findings highlight the delicate balance between HH signaling and antagonism as a critical determinant of lingual epithelial specialization and function. Further studies are needed to elucidate how HHIP modulates postnatal FILIFP development and HH signaling, with implications for diseases such as hairy tongue and glossitis.

271 **Umami Taste Detection In Children Versus Adults**

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Adults and children live in different sensory worlds. While children are less sensitive to detecting sweetness and more sensitive to detecting bitterness than adults, there is surprisingly little research using the same methods to compare their sensitivities for other tastes—particularly for umami. Here, we conducted a secondary analysis of data from children (8-14 years; n=85) and adults (21-67 years; n=71) to determine whether there are age-related changes in taste sensitivity for monosodium glutamate (MSG). Using identical procedures for both groups, MSG detection thresholds were determined via a two-alternative, forced-choice paired comparison tracking procedure previously validated for use in children. Because obesity is associated with reduced MSG sensitivity in adults, we also examined MSG thresholds as a function of body adiposity. Body fat percentage was estimated using bioimpedance electrical analysis in the majority (75%) of participants and dual-energy X-ray absorptiometry in a subset of adults. We found that, like sweet taste, children were less sensitive to detecting MSG than adults (log means of -2.74±0.04 vs. -2.86±0.04 in children vs. adults, respectively; ~2.4mM vs. 1.9mM MSG $P<.05$). Additionally, we observed a trend for age group to interact with adiposity ($P=0.08$). Adults with excess adiposity were less sensitive to MSG than those without excess adiposity (-2.79±0.06 vs. -3.03±0.10; ~2.3mM vs. 1.3mM MSG $P<.05$). However, no such differences were observed among children. While the mechanisms behind children's reduced sensitivity to detect the nutritive tastes of umami and sweet—and the lack of an association with adiposity— remain unknown, we hypothesize that higher metabolic demands for growth during development interact with the taste system. Future studies are needed.

273 **Longer In-Utero Development Leads To Enhanced Functional Connectivity And Postnatal Experience-Dependent Refinement Of The Olfactory Network**

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The sense of smell begins to function already in utero and continues to mature after birth as a crucial sense for infant-parental bonding. Animal models suggest a two-stage process for the development of the olfactory cortex; prenatal increase in neural connectivity followed by postnatal pruning and specificity. However, whether maturity or birth triggers this transition is not known. Here we aimed to determine whether this developmental pattern occurs in the human neonatal olfactory system and whether maturity or birth itself triggers the transition between stages. We utilized data from the Developing Human Connectome Project consisting of resting-state functional MRI scans of infants (n = 777), including both full-term and preterm births. In term-born infants (n = 501), a longer duration of in-utero development was associated with increased functional connectivity both within, and from, regions within the olfactory cortex. Critically, increased postpartum time was associated with a decrease in functional connectivity of the olfactory system, thereby supporting the existence of a two-stage process for olfactory development in typically developing neonates. Although preterm-born neonates had a similar increase in neural connectivity aligned with longer time in utero, that increase was weaker, compared

with infants born at full term, and did not reach the optimal level to initiate pruning. These findings provide insights into the developmental patterns of primary olfactory networks in human neonates, shedding light on the dynamic processes occurring during early olfactory system maturation.

275 **Molecular Mechanisms Shaping Taste Receptor Differentiation In Sweet And Bitter Receptor Lineages**

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Taste buds detect a wide range of flavors using specialized taste cells. Among these, type II taste cells mediate umami, sweet, and bitter tastes via distinct G-protein coupled receptors (GPCRs), specifically T1Rs and T2Rs. Key signaling molecules such as Skn-1, TRPM5, and PLCβ2 are essential for detecting sweet, amino acid, and bitter stimuli. However, the molecular mechanisms driving the differentiation of progenitor cells into distinct sweet- and bitter-detecting lineages remain unclear. Using single-cell RNA sequencing (scRNA-seq) on circumvallate papillae, we identified distinct cell clusters characterized by sweet- and bitter-specific biomarkers. Among several transcription factors identified through motif analysis and cell type-specific gene expression, Fezf1 stood out as exclusively expressed in bitter receptor cell clusters, suggesting its potential role in lineage specification. We hypothesize that Fezf1 plays a crucial role in the differentiation of progenitor cells into bitter taste receptor cells. This preliminary analysis sets the stage for further investigation using complementary approaches to elucidate the molecular pathways governing taste receptor cell differentiation.

277 **Regenerative Potential Of Cannabidiol In Chemically-Ablated Olfactory Epithelium**

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Cannabidiol (CBD), a non-psychoactive compound of *Cannabis*, has been implicated in promoting neurogenesis in the central nervous system. This study investigated whether CBD enhances olfactory sensory neuron (OSN) regeneration and functional recovery following methimazole (MeZ)-induced anosmia. OMPtauGFP male mice were orally administered 100 mg/kg CBD in jam daily for two weeks before a single MeZ injection (75 mg/kg) and throughout the 30-day recovery period. Using the buried-cookie test, MeZ-treated mice exhibited anosmia but there was no main effect of CBD drug on cookie retrieval (2-w mixed factorial ANOVA, $p = 0.4096$). CBD, however, did increase the main olfactory epithelial thickness at 10 days (CBD = 42.50 + 1.97 μm vs. Control = 36.12 + 2.76 μm; Student's *t*-test, $p = 0.0411$), an effect absent at 30 days ($p = 0.1610$). There was no significant difference in OSN density during recovery (2-w ANOVA, p = 0.1556) nor changes in Cas3 immunolabeling as a marker for cell death as sampled at day 30 (Student's *t*-test, $p = 0.1301$). We are currently sampling whether there are CBD-induced changes in neurogenesis at an intermediate time point of 15 days post MeZ ablation. Currently our findings suggest a transient effect of CBD on epithelial structure, and no substantial influence on mature OSN lifespan or olfactory recovery based upon timing of functional anosmia.

279 **The ROLe Of CHromatin STructure In REgulating VOmeronasal REceptor EXpression**

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Mouse vomeronasal sensory neurons (VSNs) detect chemical signals present in the environment using G-protein coupled receptors from three families: the type I and type II vomeronasal receptors (V1Rs and V2Rs), and the formyl peptide receptor family (FPRs). The expression of vomeronasal receptors is tightly controlled, with singular monoallelic expression characterizing V1Rs and coordinated co-expression characterizing V2Rs, but little is known about the gene regulatory processes that control receptor choice. Here, we elucidate the role of chromatin structure and 3D genome folding in regulating vomeronasal receptor expression. We identify candidate regulatory DNA elements active in the vomeronasal organ using ATAC-seq and ChIP-seq from whole VNO tissue. We then use single-cell multiome profiling to identify regions of open chromatin and sequence motifs associated with each class of vomeronasal sensory neuron. In parallel we have used Hi-C to map the spatial organization of the genome in purified vomeronasal sensory neurons, which has allowed us to generate genome-wide maps of regions of open and closed chromatin and topologically associating domains. By combining these data sets we have identified candidate regulatory elements for the regulation of vomeronasal receptor gene choice.

281 **The Impact Of Maternal High Fat And High Saccharin Diet On Offspring Taste Processing**

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Experience and the integration of sensory information work together to modify behavior. These experience-related changes in both behavior and neural circuitry have been historically highlighted in both adulthood and development. Research in experience-expectant learning has shown that the neurotypical development of the visual and auditory sensory systems is highly dependent on early life experiences with sound and light, sometimes as early as in the womb. There has been comparatively less research on the impacts of experience on the development of chemosensory systems. The impact of experience on the development of the taste system is

important to explore since olfactory and gustatory experiences play a significant role in survival, wellbeing, and quality of life.Here, we test how experience with a high fat diet (HFD - Research Diets INC 60% Kcal from fat) or a control-fat diet (Research Diets INC 15% Kcal from fat) supplemented with high saccharin consumption (HSD – ad lib consumption of 0.0055M saccharin) experienced through the mother during gestation and lactation impacts sucrose-related cFOS expression in gustatory cortex in adolescent Long Evans rat offspring (n = 41) as compared to controls. We report a statistically significant difference in weight, blood glucose, and sucrose consumption for the HFD and HSD groups when compared to controls. We also report a significant increase in sucrose-related cFOS activity in gustatory cortex following HSD and a decrease following a HFD when compared to controls. These findings suggest that food and taste experiences occurring during specific periods of early development hold a developmentally unique significance for later taste processing.

283 **Behavioral Responses To Caffeine Are Not The Same As Those We See To Other Bitters.**

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Bitter stimuli are often associated with toxicity and can be aversive. However, we consume many bitter foods in our daily lives such as healthy vegetables or coffee. Our laboratory has shown that access to a non-bioactive (non-toxic) bitter, such as quinine, decreases both meal size and rate of feeding in rats. Over time, the animals increase acceptance of the diet and rate feeding increases to near baseline. In the current experiment, we explored the behavioral response of rats to a bioactive bitter diet, caffeine. Male long Evans rats were given either a non-bitter control diet or a diet containing 0.03% caffeine ad libitum. Animals on the caffeine diet decreased 24-hour food consumption and meal number (p's<0.05) compared to controls. Animals on a caffeine diet also decreased rate of feeding upon first presentation but increased above baseline feeding rate overtime (p=0.054). They also increased meal size over time (p=0.008), the increases in rate and meal size are contrast to our work with other bitter diets. We also saw changes in the animal's drinking behavior. Caffeine treated animals drank more water and had more drinking bouts (p's<0.05) than controls. We collected saliva throughout the experiment and will compare salivary protein expression between caffeine and control treated animals.

285 **Non-Monotonic Psychometric Functions For Phenyl Ethyl Alcohol.**

E. Leslie Cameron[1], Natalie Scalamera[1], Brooke Bastian[1], Shima T. Moein[2], Richard L. Doty[3]

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Phenyl ethyl alcohol (PEA, a rose-like smelling odor) is one of the chemicals most widely used to determine olfactory thresholds. To our knowledge, no published data of its psychometric function have been reported. For some other chemicals (e.g., alpha-ionone, amyl acetate), olfactory psychometric functions are non-monotonic, exhibiting significant 'notches' at points along the function (Cameron et al., 2024; Marshall & Moulton, 1981; Cameron & Doty, AChemS, 2018; 2019). Trial-by-trial confidence tends to increase as concentration increases, generally mirroring performance (Cameron et al., 2024). In this study, we determined psychometric functions for PEA using a 2-alternative forced choice detection task that employed Sensonics' Snap & Sniff® wands or Pop and Sniff® inhalers. On each trial, two stimuli were presented in rapid succession. One contained PEA at one of 10 predetermined concentrations and the other an odorless diluent. The participant's task was to indicate which stimulus seemed stronger and to rate the degree of their confidence on a 9-point rating scale. In one condition, 14 undergraduates (3 M, 11 F) completed a single 30-minute test session of 60 trials. In another condition, 2 adults (1 M, 1 F) and 2 teenagers (1 M, 1 F) each completed 10 identical test sessions. As observed for other odorants that have been tested, consistent 'notches' at two concentrations were found using both types of stimulus presentation devices. Moreover, confidence increased exponentially with concentration and typically mirrored performance. Such discontinuities may provide insight into the underlying mechanisms involved in receptor-level processing and may explain some of the variability noted in point estimate threshold values.

287 **Improving Olfactory Sensitivity Detection Using TreesClassification**

Prasanna Karunanayaka[2], Pemantha Lakraj[1], Senal Peiris[2]

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Introduction: Olfactory function plays a critical role in daily life, offering advantages such as enhanced threat detection (e.g., environmental hazards, smoke), improved social interactions, and heightened flavor experiences. However, the ability to smell declines with aging and neurological conditions such as Alzheimer's and Parkinson's disease. Therefore, developing quick and reliable tools to assess olfactory function is essential in order to detect those changes. Method: Höchenberger et al. (2019) introduced a Bayesian adaptive algorithm called QUEST for estimating olfactory sensitivity using Sniffin' Stick data. Their study compared sensitivity thresholds derived from QUEST with those obtained through a standard staircase method. Their findings revealed substantial overlap between the two methods, with QUEST demonstrating slightly higher test-retest correlations, reduced measurement variability, and had a shorter testing duration. Building on their work, we incorporated tree classification techniques, including Partial Tree and Partial Random Forest, to further refine threshold estimation under Staircase and QUEST methods. Results: Based on simulation results, there are significant differences between mean thresholds of the staircase, partial tree and partial random forest methods. Mean threshold of partial random forest and partial tree are higher than that of staircase Conclusion: Incorporating tree classification techniques can be a robust approach for olfactory threshold assessment. Further research, however, is needed to optimize these techniques for assessing olfactory performance.

7:00 - 9:00 PM	Calusa EFGH
Award Lectures	

Chair(s): Yanina Pepino

7:00 **Achems Young Investigator Awardee**

7:30 **Lawless Award For Research Excellence In The Psychophysics Of Human Taste And Smell**

8:00 **Ajinomoto Awardee**

8:30 **Max Mozell Awardee**

Saturday, April 26, 2025

7:30 - 9:00 AM	Estero Foyer
Continental Breakfast	

8:00 - 10:00 AM	Estero Ballroom
Poster Session V	

300 **Detection Thresholds To Glucose, But Not Other Sweeteners, Differ Between Fasted And Fed States**

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Glucose is the principal source of energy for humans. As such, the ability for the body to sense glucose is critical for maintaining energy homeostasis and is particularly important when an individual needs energy. We first investigated whether humans are more sensitive to glucose when they are fasted versus fed, and whether this would translate to other sweet-tasting compounds. Overnight fasted participants (N = 27; 17 M, 10 F) attended three sessions where their oral detection thresholds to glucose, fructose, and sucralose were measured before and after consuming a provided meal until full (295-1475 kcal). During each session, the detection threshold to one of the three compounds was measured using 3-AFC tests following a modified staircase method. We found that individuals were more sensitive to glucose when they were fasted compared to fed (paired t-test, $p < 0.05$). However, this effect did not translate to fructose and sucralose ($p > 0.05$). Additional experiments are currently underway to investigate whether sodium-glucose cotransporter-1 (SGLT1) contributes to this selective sensitivity to glucose using an inhibition/enhancement paradigm.

302 **Bitter Battles: The Tale Of Bitter Perception And Its Neuronal Underpinning**

Oren Mazon[1], Dan Ben-Ezra[1], Ron Gerbi[1], Anan Moran[1,2]

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The bitter taste sensation serves as a defense mechanism against harmful compounds, while also contributing to the complexity of culinary experiences and potentially signaling medicinal benefits. It is surprising, however, that both the question of whether bitterness is a unified (monoguesic) or a complex sensation, and its system-level underpinning remain unresolved. Behaviorally, rats showed a complete failure to distinguish between briefly sampled bitterant pairs when intensity is removed as a cue. In humans, while bitterants discrimination is still a difficult task, it was shown that some bitterants can be classified differently from others. Interestingly, the overall-accepted bitterness monoguesic perception hypothesis is at odds with results from neuronal activity studies, mainly from early nodes of the taste system, that showed distinct responses to different bitterants. Here we combined rat behavioral bitterant preference tests with electrophysiological recordings from lower and higher brain regions of the taste system to study the logic of the bitter perception and coding. Our results show that given a longer sampling time (10 minutes), rats significantly preferred denatonium over quinine, and quinine over sucrose octaacetate (SOA); a preference relation that was maintained across days. Preliminary electrophysiological recording using Neruopixels probes from the gustatory cortex (GC) showed distinct neuronal responses to iso-intense bitter tastes. Our results suggest that bitterness is not as monoguesic perception as was previously suggested, which is probably supported by distinct activation in different regions of the taste system.

304 **A Novel Approach To Investigating Anticipatory Cortical Responses To Taste Associated Cues**

Emma A Barash, Usha Berger, Donald B Katz
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Survival is inextricably tied to consumption decisions; ingestion of toxic foods cause illness/death, while nutrient-rich foods promote health. Thus, it is paramount to understand how food cues (e.g., the color of a fruit) guide approach-avoidance decisions regarding potentially nourishing (or sickening) foods. While cue-driven-association research is common, it is still unclear whether cue-associations evoke sensory codes. To bridge this gap, we created a novel experimental framework aimed at training cue-food reward associations in an electrophysiology-friendly manner that enables us to separate the effects of a reward's valence from its identity. We designed a paradigm featuring cue-trigger/retrieval-reward sequencing, pairing visual-auditory cues with unique chemosensory taste concentrations — palatable sucrose and sodium chloride, and aversive sodium chloride. Across several sessions, rats come to subtly adapt their approach or avoidance to cues based on reward palatability. As satiation increased during sessions, individual preferences emerged even among the palatable

options, leading to stratification in total consumption by the session's end. Preliminary electrophysiological data from gustatory cortical (GC) neurons reveal, prior to taste delivery, clear responses that predict GC responses to the tastes themselves, but in reverse—strong taste responses predicted by weak cue responses, and vice-versa. Integration of behavioral and electrophysiological data allows us to investigate how the neural encoding of "anticipatory responses" in GC correlates with true taste responses in terms of identity and palatability.

306 **Odor Discrimination In Detection Canine Training: Analyzing The Volatile Organic Compound Profile Of Virus And Heat-Stressed Cell Culture Samples**

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Canines have long been employed for odor detection due to their advanced olfactory machinery, and more recently expanding biodetection applications include pathogenic and disease surveillance. While the effort toward demonstrating canine biosensor capacity grows, it is also important to elucidate molecular profiles associated with biological targets of interest to optimize training materials and simultaneously build predictive odor recognition models. In this work, proton transfer reaction-mass spectrometry (PTR-MS) is used for online volatile organic compound analysis of a cell culture-cultivated viral target, channel catfish virus (CCV) 6.25 x 10^8 CCID50/ml, and alternative biological distractor samples used for canine odor discrimination including healthy uninfected channel catfish oocyte (CCO) host cells, heat stressed CCOs, and fathead minnow epithelial (FHM) cells. Supernatant containing the cell lysate from each culture condition was collected for replicate headspace analyses and the extracted ion chromatogram revealed peak signatures unique to both healthy cell lines. CCOs under different types of physiological stress had similar profiles which included compounds related to oxidative stress responses, including ethylene, hydrogen peroxide, nitric oxide, and formyl radicals with varying signal intensity. However, there were several peaks unique to each stressor, and cell lysate from virus-infected cells indicated elevated alkalinity, which is thought to be one mechanism of programmed cell death. This work highlights the complexity of biological odor profiles and the importance of careful distractor selection in odor learning.

308 **Investigation Of The Pharmacodynamic Properties Of Tas1R2/Tas1R3(T1R2/R3) Ligands With Distinct Binding Sites Using Rapid Throughput Taste Discrimination With Human Subjects**

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T1R2/R3 is a class C heterodimer GPCR, with multiple binding sites across both TAS1R2 and TAS1R3 protomers that accommodate many different ligands, of various pharmacological actions, from a broad array of chemical classes. With so many pharmacological tools available, human sweet taste behavior should be an ideal model to study principles of receptor pharmacodynamics in vivo. The TāStation® is a rapid throughput, operant taste discrimination technology with the capacity required for carrying out robust concentration-response analysis of human tastant receptor ligands. We are using TāStation® to pharmacologically characterize human taste response to agonists, antagonists, and positive- and negative-allosteric modulators (PAMs and NAMs) operating at different binding sites on T1R2/R3. Concentration-response analysis of the saccharide sweeteners sucrose, fructose, glucose, and sucralose, all of which bind to a site in the amino terminus "Venus flytrap domain" (VFD), yielded EC50s of 33, 118, 127, and 0.08 mM. FEMA 4774, a T1R2/R3 PAM in vitro, at 0.03 mM decreased sucrose EC50 and Hill coefficient values approximately 2.5-fold. However, 0.03 mM FEMA 4774 had no measurable impact on fructose and glucose concentration-response functions. Lactisole, a T1R2/R3 NAM with a binding site located in the transmembrane domain of the TAS1R3 protomer, eliminated taste responses to all but the highest concentrations of sucrose, fructose, and glucose. Cyclamate also binds to this site, but at 0.1 mM interacted synergistically with sucrose, and exhibited intrinsic agonist activity at 0.2 and 0.4 mM. Studies of lactisole, FEMA 4774, and cyclamate effects on T1R2/R3 agonists with binding sites elsewhere on the receptor are ongoing.

310 **Sex Differences In Rats&Rsquo; Olfactory Behavior Depend On Behavioral Context**

Leslie M. Kay[1,2], Sam Detwiler[2], Nasya Becton[3], Kruthika V. Maheshwar[4], Nadia Turki[4], Emma Bell[3], Brian J. Prendergast[1,2]

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Since 2015, when the NIH mandated consideration of sex as a biological variable, many olfactory studies include both sexes, but few are explicitly designed to test sex differences. We present here tests of sex differences in odor-guided behavior and olfactory bulb (OB) neurophysiology. We compared go/no-go (GNG), 2-alternative choice (TAC), and odor habituation behavior in Long Evans male and female rats. In both operant tasks, males and females perform at equivalent levels, but the two sexes use different odor sampling and other behavioral strategies to maintain these performance levels. In GNG and 3 versions of a TAC task, separate groups of rats show that females sample odors for 75-125 ms longer than males, with the difference dependent on the task. Furthermore, males sample about 75 ms longer in GNG than TAC, replicating our earlier study, but females sample the same length of time in both tasks. Females also achieve peak performance over a wider range of sampling times than males. Both males and females also show variability in odor sampling times during GNG across the day, sampling significantly shorter in the early and longer in the later part of the light phase, with a larger effect in females than males. In an odor habituation task, females sample about one second shorter than

males after habituation. In this study, we also monitored the OB local field potential and found that females' gamma (65-120 Hz) and beta (15-30 Hz) oscillations are lower in amplitude than males' during, but not outside of, odor sampling. We tracked estrus in the GNG and habituation studies and found no correlation of any behavioral or physiological measures with estrus in females. We also found that variance for each of our measures was not different across the two sexes.

312 **Taste Perception Of Sugar-Free Isomaltooligosaccharides**

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Studies in our lab have previously reported that maltooligosaccharides (i.e., gluco-oligosaccharides (GlcOS) containing α-1,4 glycosidic linkages only) elicit a "starchy" taste. This study aimed to investigate the taste property of GlcOS that predominantly consisted of α-1,6 glycosidic linkages. Sugar free, food-grade samples were prepared via ethanol fractionation from two commercially available mixtures, maltosyl-isomaltooligosaccharides (MIMO) and isomaltooligosaccharides (IMO). The resulting samples were composed of 4 – 7 glucose units with different structural characteristics; α-1,6 linkages accounted for ~75% of the total bonds in MIMO and ~50% of the total bonds in IMO. When tested at 150 mM, subjects (N = 28) could discriminate MIMO and IMO from blanks ($p < 0.05$) and described these samples as "slightly sweet". Their detectability was comparable to that of 150 mM maltose. The subjects could not discriminate the samples ($p > 0.05$) in the presence of lactisole. When tested at 75 mM, subjects (N = 25) could discriminate MIMO and IMO from blanks ($p < 0.05$) but found it challenging to describe the taste of these samples. Their detectability was, however, comparable to that of 75 mM glucose and maltose. This study confirms that glycosidic linkage configurations play a role in modulating taste perception of GlcOS.

314 **Noxious Spinal Stimulation Activates Taste Neurons In The Parabrachial Nucleus**

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Our lab recently found that taste neurons in the parabrachial nucleus (PbN) show responses to oral somatosensory stimuli. It is unknown whether PbN taste neurons respond to a broader array of stimuli such as spinal dorsal horn input that reaches the PbN. Here, we used optogenetic and electrophysiologic methods applied to a mouse model generated by breeding male TRPV1-Cre and female Cre-dependent ChR2 reporter mice. PbN cells were recorded under anesthesia during oral chemical and thermal stimulation and spinal somatosensory stimulation. Taste responses (spikes) were indexed using temperature-controlled solutions of (in mM) 100 NaCl, 500 sucrose, 10 quinine, 0.1 cycloheximide, 10 citric acid, and an umami mixture. Somatosensory stimuli included oral thermal stimuli (water at 8 different temperatures, from extreme cold oral ~7° to noxious heat 51°C), 1 mM allyl isothiocyanate (AITC; agonist of TRPA1 and TRPV1), 1.28 mM menthol (TRPM8) and 1 mM capsaicin (TRPV1). Noxious spinal stimuli were applied by pinch to the hind paws and tail with calibrated forceps. A 473 nm laser was applied to the receptive field defined by pinch stimulation. Analyses of 34 PbN neurons identified (6 units were not completed across all trials), ten units were activated by more than one mode of stimuli among which one cell was activated by bitter taste, AITC and pinch to the hindpaw/tail. Interestingly, we found 3 taste neurons which were activated by pinch to the paw/tail but not oral somatosensory stimuli, indicating lack of hierarchy ranking for their possible convergence. Our data appear to support there is a shared common dimension across multi-sensations coded in PbN. This study is still ongoing, with an emphasis on searching more cells accounting for this broad multisensory convergence.

316 **Serotonergic Sem-1 Neurons Modulate Feeding Behavior In *Drosophila Melanogaster***

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Feeding behavior is essential for survival and is tightly regulated by neural circuits integrating sensory inputs and internal states. Serotonin (5-HT) is a conserved neuromodulator involved in feeding regulation across species. In *Drosophila melanogaster (fruit fly)*, serotonergic neurons in the subesophageal zone (SEZ) play critical roles in processing taste signals and modulating feeding behavior. Our study investigates a subset of SEZ serotonergic neurons, the SEM-1 neurons, and their role in feeding regulation. Using intersectional genetics, we identified drivers that label SEM-1 neurons, enabling morphological and functional analyses. SEM-1 neurons densely innervate the anterior-ventral SEZ. Calcium imaging revealed that SEM-1 neurons selectively respond to sugar taste detection but not to bitter or water. Interestingly, SEM-1 neurons are inhibited by sugar detection on the proboscis, suggesting that their neural activity is suppressed during sugar feeding. Disrupting their suppressed activity during sugar feeding—by artificially activating them using optogenetics—did not affect feeding initiation but resulted in decreased sugar intake. These results suggest that SEM-1 neurons provide inhibitory control over food ingestion, and that sugar taste detection relieves this inhibition by suppressing SEM-1 activity. Ongoing work utilizes the fly brain connectome to identify SEM-1 synaptic partners and neural circuits involved in taste processing and feeding regulation. We are also examining the potential influence of hunger and satiety on SEM-1 activity. Our studies establish SEM-1 neurons as key modulators in serotonergic regulation of feeding, providing insights into how neuromodulation supports adaptive behavior in response to sensory and internal cues.

318 **Postsynaptic Targets Of Central Amygdala Axon Terminals In The Nucleus Of Solitary Tract.**

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The rostral third of the nucleus of solitary tract (NST) is the first central synapse for neural processing of gustatory information that can be modulated by descending input from several forebrain areas. For example, electrical activation of the central nucleus of the amygdala (CeA) concurrent with taste stimulation of the anterior tongue has been shown to increase neural responses. Given that CeA projection neurons are primarily GABAergic and the NST is rich in GABA positive neurons, we hypothesize that CeA axon terminals in the NST synapse with GABAergic neural elements. Such an organization would suggest that CeA-induced augmentation of taste-evoked responses recorded in the NST might result from inhibition of intrinsic GABAergic cells that, in turn, synapse with taste-responsive NST neurons. To test this hypothesis, we injected transynaptic AAV-Cre virus in the CeA of vesicular GABA transporter (VGat) triple transgenic mice (VGat-FlpO/frt-TdTomato/loxP-EYFP). Additional experiments used similar injection of transynaptic AAV-Cre in the CeA of VGat-FlpO/frt-TdTomato double transgenic mice combined with Cre-dependent AAV-EYFP virus injected into the NST. Quantitative analysis of transynaptic EYFP-labelled cells in the NST indicates that CeA axon terminals synapse, almost exclusively, with non GABAergic NST neurons. Thus, the predominant excitatory influence of CeA activation on taste-evoked responses recorded in the NST is not easily explained through disinhibition. In fact, the principle targets of these NST neurons is the contralateral NST and parvocellular reticular formation as well as the ipsilateral parvocellular reticular formation and parabrachial nucleus, suggesting that CeA axon terminals in the NST synapse with glutamatergic projection neurons.

320 **Largely Separate Populations Of Somatostatin Expressing Cells In The Central Nucleus Of The Amygdala Project To The Nucleus Of Solitary Tract, Parabrachial Nucleus, And Bed Nucleus Of The Stria Terminalis.**

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The nucleus of solitary tract (NST) and parabrachial nucleus (PBN) represent the first and second central synapses for ascending gustatory information. Neural processing of taste information in these nuclei is influenced by descending input from forebrain regions such as the central nucleus of the amygdala (CeA), lateral hypothalamus (LH), and bed nucleus of the stria terminalis (BNST). We have shown that CeA somatostatin (Sst) expressing neurons projecting to the NST, PBN, and LH are largely distinct cell populations. The present experiments tested the premise that this organizational scheme extends to CeA output to the BNST, NST, and PBN. In Sst-Cre mice, we injected different fluorescent retrograde viral tracers into the NST and BNST or into the PBN and BNST. Quantitative analysis of retrograde-labelled cells in the CeA showed that CeA/Sst cells projecting to the NST or PBN are largely distinct from those projecting to the BNST. Together, our anatomical results highlight the importance of targeting a defined projection of CeA/Sst neurons rather than simply targeting the whole population when assessing function.

322 **Peripheral Gustatory Neurons Primarily Function To Categorize Stimuli Into Three Groups**

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It is well-established that some peripheral taste neurons are narrowly tuned, while others are broadly tuned. How these distinct tuning properties contribute to gustatory coding remains less clear. To address this question, we recorded calcium responses from 280 geniculate ganglion neurons in response to taste stimuli. Examination of the responses of these neurons to five stimuli representing the basic taste categories revealed that 47% responded to a single stimulus (narrowly tuned) and 53% responded to more than one stimulus (broadly tuned). When hierarchical cluster analysis was performed using five taste stimuli, geniculate taste neurons were divided into five functional groups. However, when seven stimuli were used, the neurons were divided into six functional groups. This finding indicates that the number of functional clusters for gustatory neurons depends on the number of stimuli used in the experiment. A principal components analysis revealed that taste stimuli are consistently categorized into three groups, regardless of whether five or seven stimuli are examined. The first category consisted of bitter, sour, and non-sodium salts, which are aversive stimuli. The second category included sucrose and umami, which are caloric. The third category comprised sodium salts, which can be either aversive or appetitive depending on the animal's physiological state. Both narrowly tuned neurons and some broadly tuned neurons function to place stimuli into these categories. However, 40% of the neurons responded to stimuli in more than one category. These neurons were more likely to exhibit mixture suppression than neurons responding to stimuli within a single category. Lastly, Type II cells are required to represent these three functional categories and for mixture suppression of sour/sucrose mixtures.

324 **Does Sour Stimulation Inhibit Responses To Sweet Stimuli In The Mouse Geniculate Ganglion?**

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The mouse geniculate ganglion receives input from taste buds of the anterior tongue and palate. It is hypothesized that in taste buds, sour-sensing Type III taste cells inhibit sweet-sensing Type II taste cells when a mixture of sour and sweet stimuli is applied. If this is the case, geniculate ganglion cells should respond less robustly to a mixture of sucrose/citric acid than to sucrose alone. Indeed, consistent with data from other laboratories, we found that adding 10 mM citric acid to 300 mM sucrose reduced responses in sucrose-sensing ganglion neurons to 30% (n=27 neurons, $p<0.0001$). KCl also stimulates sour-sensing Type III taste bud cells and leads to the release of inhibitory transmitters in taste buds. Thus, we reasoned that KCl, too, should reduce sucrose responses. However, inconsistent with the proposed hypothesis, adding KCl to sucrose (250 mM

KCl/300 mM sucrose) did not alter the sucrose responses in sucrose-sensing ganglion neurons. Sucrose responses in the presence of KCl were 87% of the control values, which was not a significant difference (n = 30 neurons, p = 0.09). Thus, when recorded in the geniculate ganglion, the modulation of sweet responses by acidified sucrose may or may not arise from interactions between Type II and Type III cells in the taste bud. To further explore if activation of acid-sensing Type III taste bud cells alters responses at the level of the geniculate ganglion, we are currently testing whether NH_4Cl —another taste stimulus for Type III taste cells—inhibits sucrose responses in the ganglion.

326 **Grp Signaling In Bla-Grpr Neurons Regulates Feeding Patterns By Modulating Taste Palatability**

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Feeding is not solely driven by homeostatic needs but is influenced by multimodal aspects of food, including taste palatability. Alteration in palatability perception could be reflected in changes in feeding patterns typical of eating disorders such as obesity, binge eating, and overconsumption. The gustatory portion of insular cortex (GC) and the basolateral of amygdala (BLA) are implicated in the control of feeding and taste palatability, suggesting that the GC-BLA neural circuits could be a strong candidate for investigating the neural underpinnings of eating disorders. Informed by findings about the involvement of gastrin releasing peptide (GRP) in meal termination and of GRP receptor signaling in encoding the valence of sensory stimuli, we tested the possibility that the GC-GRP/BLA-GRPR circuit is involved in changes in feeding patterns attributable in shifts in palatability. We report that BLA neurons expressing GRPR are heterogeneous and receive a dense projection from GRP-expressing neurons in GC. Taking advantage of optogenetics combined with patch clamp, we investigated the effect of GRP modulation on both membrane properties of GRPR neurons and on evoked responses from GC terminal fields in BLA. Finally, we investigated the effect of local GRP infusion in GC on feeding patterns. These results identify a neuropeptide-defined circuit mediating direct GC-BLA interactions and regulating eating patterns.

328 **Fostrapping Neural Networks Driven By Odor Stimulation**

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Mitral/tufted cells not only serve to output olfactory information, but are now known to project to downstream sites regulating energy balance at specific hypothalamic nuclei. Herein, we employed Fos-TRAP (targeted recombination in active populations) to functionally map neuronal populations in the brain that are active following odor stimulation. Male and female Fos2A-iCreER (TRAP2) mice were stimulated with isopropyl tiglate in a custom olfactometer using a cyclic pattern of odor stimulation. Using the olfactory bulb as a positive control, we observed an abundance of FOSTRAP neurons in the granule cell layer (***$p<0.001$), and moderate activation in the mitral cell layer (**$p<0.01$) in odor-stimulated mice. Significant activation was seen in both anterior and posterior piriform cortex subdivisions (**$p<0.01$). Discrete activation pattern was observed in the hypothalamic arcuate nucleus, paraventricular hypothalamic nucleus, dorsomedial hypothalamic nucleus, supramammillary nucleus and lateral hypothalamus (**$p<0.01$). Specific dendritic spine labeling in hippocampal granule and pyramidal neurons suggests a novel method to study plasticity in active neurons. Using Tbx21-cre mice with restricted EGFP expression in mitral and tufted cells, we screened downstream neural connectivity and observed axonal varicosities near c-Fos immunoreactive cells in the accessory olfactory bulb and cortical amygdala. Probing for calretinin in the olfactory bulb and oxytocin/vasopressin in the paraventricular nucleus revealed minimal co-expression with FOSTRAP/c-Fos, suggesting alternate activated populations in these areas. This study demonstrates that the FOSTRAP approach is a convenient tool for mapping odor-activated pathways in the brain.

330 **Regulation Of Breathing And Sniffing By The Locus Coeruleus In Mice**

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As a vital sign, breathing is constantly modulated by external stimuli and internal states. Sniffing, a distinct breathing pattern, is essential for animals to navigate the environment, and in rodents, it entails an integrated action including high-frequency breathing. Sniffing can be triggered by odors and other salient stimuli or occur spontaneously, reflecting an internal drive for exploration. However, the neural mechanisms that regulate sniffing under different behavioral contexts remain largely unknown. Here we hypothesize that the locus coeruleus (LC) is involved in the regulation of sniffing given its role in mediating arousal and its reciprocal connections with the preBötzinger Complex (preBötC), a breathing center in the brainstem. We used the dopamine b-hydroxylase (DBH)-Cre mice to gain genetic access to LC noradrenergic neurons. Via Ca^{2+}-based fiber photometry in freely behaving mice, we found that the activity of LC neurons is temporally coupled to sniffing, either spontaneously occurred or triggered by external stimuli in different sensory modalities (e.g., odor presentation, light-dark transition, and marble drop). Moreover, chemogenetic inhibition decreased the breathing frequency in response to salient sensory stimuli in a task-dependent manner. Finally, optogenetic activation of LC neurons increased the breathing frequency under anesthesia but not in wakefulness. These results suggest that LC noradrenergic neurons regulate breathing/sniffing in a state- and context-dependent manner.

332 **Navigating The Where And What? Δ-Protocadherins Are Critical For Vomeronasal Neuron Targeting In The Accessory Olfactory Bulb**

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The assembly of functional neural circuits is a highly coordinated process that requires precise control over axon guidance and selective cell-cell interactions. Our understanding of how neurons identify, select, and connect to suitable synaptic partners remains incomplete. Altered neuronal connectivity has been linked to significant neurological disorders, including autism and schizophrenia. Our research aims to unravel the mechanisms involved in neuronal guidance and cell-cell interactions by studying the accessory olfactory system (AOS) in rodents, which includes the vomeronasal organ (VNO) and the accessory olfactory bulb (AOB). Utilizing mouse genetics and single-cell transcriptomics, we examined the role of non-clustered/δ-protocadherins in neuronal spatial segregation and connectivity. Our findings indicate distinct combinatorial expression patterns of non-clustered protocadherins in vomeronasal sensory neurons (VSNs) that express different vomeronasal receptors and their target cells. Furthermore, our data highlight the crucial role of the δ-protocadherin repertoire in axon guidance and connectivity within the AOB. Specifically, observations regarding Pcdh7 and Pcdh9 reveal that they compromise regional axon segregation and affect the number and size of glomeruli formed by VSNs with their targeted mitral cells (MCs). Additionally, observations from Nrp2 knockout (KO) mice suggest that Semaphorin III-mediated axon segregation in the AOB may have epistatic interactions with δ-protocadherins. Overall, our research provides important insights into how changes in protocadherin expression or function can shape the connectivity of chemosensory neurons to the brain.

334 **Odor Stimulation Enhances Hypothalamic *C-Fos* Expression In Kv1.3 -/- Mice**

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Due to the well-documented link between olfactory bulb activity and the regulation of metabolism, we utilized Kv1.3-/- mice (KO; voltage-gated potassium channel) to examine altered functional connectivity between the olfactory bulb and hypothalamus. Because KO mice are thin without caloric restriction and resistant to diet-induced obesity, we hypothesized they would have enhanced functional connectivity between these regions. Wildtype (C57BL6/J, WT) and KO mice (n=6/genotype) were stimulated with1 mM isoamyl acetate using a custom olfactometer delivering cyclic stimulation, followed by traditional *c-fos* immediate-early gene immunolabeling. We report a genotype independent, main effect of odor stimulation in the glomerular layer (2w ANOVA, $p = 0.019$). Moreover, KO mice had increased odor-evoked *c-fos* labeling over that of WT in both the mitral cell and granule cell layers (2w ANOVA, MCL: $p < 0.0001$; GCL: $p = 0.0002$). Brain-wide *c-fos* activation was mapped (n=3/genotype) using tissue clearing and lightsheet microscopy. Computed 3D *c-fos* density maps were generated using ClearMap and compared within genotype (Student's *t*-test). KO mice exposed to odor showed higher *c-fos* expression in numerous downstream targets compared to WT mice. *C-fos* activity was analyzed in several energy-sensing regions of the hypothalamus, including the paraventricular hypothalamus (PVH), the dorsomedial hypothalamus (DMH), and the arcuate hypothalamus (ARH). *C-fos* activity in the PVH was markedly enhanced in KO mice, yielding an odor-genotype interaction (2w ANOVA, $p = 0.025$). Our study reveals coactivation between the olfactory bulb and energy regulating regions of the hypothalamus. We conjecture that resistance to diet-induced obesity may be mediated by the PVH; a region known to operate in neuroendocrine function.

336 **Representation Of Taste-Related Neural Activity In The Mouse Mediodorsal Thalamus**

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The decision to consume certain foods depends on the taste and the reward experienced while eating. This information is processed through neural computations in interconnected gustatory regions. The mediodorsal nucleus of the thalamus (MD), which is not part of the canonical taste pathway, is a multimodal brain area connected with gustatory centers and has been shown to represent intraorally-delivered chemosensory stimuli after strong retronasal odor-taste associations. Key questions remain about whether MD neurons can process taste quality independently of odor-taste associations and how they represent extraoral signals that predict rewarding and aversive outcomes. Here, we use chronic silicon probes to record neural activity in the MD of actively licking mice. Mice were presented with taste stimuli (sucrose, NaCl, citric acid, quinine, or water) at room temperature. Given the MD's involvement in anticipatory responses, we explored its role in specific expectations of rewarding (sucrose) or aversive (quinine) taste stimuli. Our data show how mouse MD neurons represent and encode 1) the identity and concentrations of basic taste qualities, and 2) auditory signals anticipating rewarding and aversive taste outcomes. MD neurons can reliably and dynamically encode taste identity in a broadly tuned manner and taste concentrations with spiking activity positively and negatively correlated with stimulus intensity. Our data also show that MD can represent information related to predictive cues and their associated outcomes, regardless of whether the cue predicts a rewarding or aversive outcome. In summary, our findings suggest that the MD is integral to the taste pathway, as it can encode sensory-discriminative dimensions of tastants and process associative information essential for ingestive behaviors.

338 **Distinct Dynamics Of Cholinergic And Gabaergic Signaling From The Basal Forebrain To The Olfactory Bulb During Odor-Guided Tasks.**

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Throughout the neocortex, basal forebrain (BF) cholinergic and GABAergic signaling are linked to aspects of goal-directed behavior, including cue detection, reward expectation, and reinforcement delivery. In anesthetized preparations, the projections from the BF to the olfactory bulb (OB) influence odor responses and OB circuits, yet their dynamics in behaving animals remain unclear. To determine the temporal dynamics of BF-to-OB projections in awake, behaving animals, we imaged acetylcholine (ACh) signaling in the OB using a genetically encoded acetylcholine sensor (GRAB-ACh4h) and recorded OB-projecting GABAergic neuronal activity from the BF using retrograde-GCaMP8m injected into the OB of VGAT-Cre mice. We trained head-fixed mice on a simple olfactory Go/No-Go task to assess BF-to-OB signaling during odor discrimination. Dynamic changes in OB ACh transmission corresponded to distinct behavioral aspects of the task, including anticipatory licking, reward consumption, inhalation frequency, and locomotion. OB-projecting GABAergic BF neurons showed more transient activation linked to odorant onset, with small but significant differences in response amplitudes for rewarded versus unrewarded odorants, with no activity changes linked to licking or reward consumption. In a novel odor presentation paradigm, we observed phasic activation of OB-projecting GABAergic BF neurons timed to odor onset that habituated over subsequent presentations. These results suggest that ACh modulation of OB circuits may reflect ongoing changes in behavioral state, whereas GABAergic modulation may be more closely linked to odor perception. Thus, different descending BF populations may differentially modulate odor information processing during behavior.

340 **The Combination Of Glucose And Saccharin Induces Higher Levels Of Licking And Nucleus Accumbens Neural Activity In Mice Compared To Either Stimulus Alone**

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The combination of the artificial sweetener saccharin (S) together with the caloric sugar glucose (G) is highly appetitive in rodents in 24-hr access tests. Here, we used brief access tests to assess licking for G, S, and G+S to determine whether this phenomenon occurs at earlier time points. To gain insight into the neural mechanisms mediating these effects, we used *ex vivo* and *in vivo* strategies to measure neural activity in the gustatory cortex and nucleus accumbens for each stimulus. Hypothesis: We hypothesized that mice lick more for G+S than either G or S alone, and that G+S stimulates elevated activity in the nucleus accumbens. Methods: Sixteen male and female C57BL/6J mice were given 4 mM saccharin and 200 mM glucose alone and in combination for 10 secs in a Davis-rig gustometer. Mice were then presented with either 4 mM saccharin, 200 mM glucose or G+S for 3 minutes with a 200 lick cap followed by immediate sacrifice. Immunohistochemistry identified pERK expression in gustatory cortex, nucleus accumbens core and shell. In a separate cohort, we performed *in vivo* dopamine recordings via fiber photometry in accumbens core to the same concentrations of sweeteners. Results: Mice licked more for the G+S in brief access tests ($p<0.05$). Mice given G+S on the day of sacrifice had significantly higher pERK immmunopositive cells in the accumbens core than those with access to either G or S alone ($p<0.05$). There were no pERK differences among stimuli in gustatory cortex or accumbens shell. Fiber photometry revealed greater dopamine signaling to G+S ($p<0.05$) in accumbens core than to either stimulus alone. Conclusions: Mice licked avidly for G+S in short term tests. G+S stimulated higher pERK signaling in the nucleus accumbens core and greater dopamine signaling than did either stimulus alone.

342 **Dopaminoceptive Circuitry Between The Ventral Striatum And Brain Regions Implicated In Sensory-Guided Behavior**

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The mesolimbic dopaminergic pathway is involved in cognitive processes and odor-mediated motivated behaviors. Within this overall network, major outputs from the ventral tegmental area (VTA) predominantly project to the ventral striatum, where they synapse on dopamine receptor expressing neurons. Other regions implicated in sensory-guided behaviors also receive input from the VTA, including the basolateral amygdala (BLA), ventral hippocampus (vHPC), and prefrontal cortex (PFC). We sought to explore the connectivity between the ventral striatum with these other dopaminoceptive regions. To determine this, we used Cre-dependent viral tracing techniques in d*rd1-, a2a-,* and *drd3*-Cre mouse lines of both sexes to investigate the circuitry of neurons which express D1, D2, and D3 dopamine receptors respectively. A Cre-dependent retrograde virus encoding for mCherry was injected into the nucleus accumbens (NAc) and a separate virus encoding for GFP was injected into the tubular striatum (TuS). Using fluorescence microscopy, we imaged and quantified the number of cells in the BLA, vHPC, and PFC that project to the ventral striatum. Results indicate that there are dopamine receptor expressing inputs to the NAc and TuS from the BLA, PFC, and parts of the vHPC. Ongoing work is investigating the proportion of neurons that express D1, D2, or D3, and what proportion of individual neurons might send projections to both the NAc and the TuS. Additionally, we are exploring the contributions of ipsilateral and contralateral BLA, PFC, and vHPC inputs to the ventral striatum. These results expand upon the established connectivity between the ventral striatum and other dopaminoceptive regions revealing potential insights into how the mesolimbic dopamine network mediates motivated behaviors that are informed by odors.

344 **_Tas2R38_ Pav/Pav Homozygotes Do Not Find _Antidesma Bunius_ Berries Bitter Tasting, Whereas Other _Tas2R38_ Haplotypes Can.**

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The bitter taste receptor TAS2R38 is activated by phenylthiocarbamide (PTC) and propylthiouracil (PROP). Two groups demonstrated that sensitivity to bitterness from *Antidesma bunius* berries was inversely correlated with the ability to taste bitterness from PTC (Henkins, 1977 & Risso, 2018). All subjects who tasted *Antidesma* extract as bitter found PTC not bitter, and those who tasted PTC as bitter found *Antidesma* not bitter. We tested a single large pedigree (n = 86) with *Antidesma bunius* berries and examined their bitterness intensity ratings. To extend previous research, we compared each subject's bitterness intensity rating of *Antidesma bunius* with their modified Harris-Kalmus bitterness recognition thresholds for PTC and PROP, as well as PROP intensity ratings. We replicated the results of previous reports. Perceived bitterness of *Antidesma* berries can be partly explained by haplotypes of the single bitter receptor gene h*TAS2R38*, which accounts for a large portion of PTC and PROP taste variability. All participants with the PAV/PAV haplotype (most sensitive to PTC) found *Antidesma* not bitter, with one exception. Conversely, half of the participants with the AVI/AVI haplotype (least sensitive to PTC) rated *Antidesma* as bitter. Whether participants with AVI/AVI found *Antidesma* bitter appears to be heritable. These data suggest that the PAV allele of *TAS2R38* prevents perception of bitterness for *Antidesma bunius* berries. Our results indicate that either TAS2R38 serves as a receptor for bitter compounds in *Antidesma* and that PAV is a non-functioning receptor or, alternatively, there is a cofactor, such as another TAS2R or a salivary protein, and the TAS2R38 PAV allele is not functional with the cofactor.

346 **Non-Canonical Detection Of Glucose And Fructose In Gustatory Afferent Neurons**

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Sweet, bitter and umami tastes are transduced via TasRs. A major effector for this signaling is phospholipase Cβ2 (PLCβ2). Additionally, certain sugars including glucose are believed to act via a non-canonical pathway independent of TasRs and PLCβ2. To examine neural signals reflecting this pathway, we recorded taste-evoked Ca^{2+} responses in geniculate ganglion afferent neurons in male and female *Plcb2*-/- (ko) mice, using GCaMP3 Ca^{2+} imaging. The non-canonical pathway has been proposed to involve a Na-dependent glucose transporter (SGLT1) and glucose metabolism in taste bud cells. Thus, we recorded responses to glucose or fructose applied at concentrations up to 1M for 30 seconds. Under these conditions, responses to these monosaccharides were indeed observed in *Plcb2* ko mice. Brief stimulation (5s) with glucose or fructose elicited responses while sucrose, a disaccharide, did only infrequently. As expected, gustatory responses to NaCl (250 mM) or citric acid (10 mM), which are not mediated via PLCβ2, showed no significant difference between *Plcb2* ko and heterozygous mice (NaCl, p=0.85; citric acid, p=0.09; n=7 ko, 6 het; Mann-Whitney). We tested the premise that these non-canonical sugar responses originate from SGLT1 on taste bud cells. We found that glucose, a known substrate, and fructose, not a substrate, both at 1M, elicited equivalent responses in gustatory neurons. Further, responses to fructose and glucose were unaffected by varying $[Na^+]$ in the stimulus solutions from 0 to 100 mM NaCl. Neurons that responded directly to NaCl were excluded in this analysis to avoid confusing the results with NaCl-evoked responses. Our results confirm that a non-canonical sweet taste transduction pathway exists for glucose and fructose, but it may rely on components other than SGLT1.

348 **Sweetness Perception And Tas1R2 Gene Expression: Insights From Sucrose, Acesulfame K, And Rebaudioside A.**

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Sweetness perception impacts dietary choices and is influenced by various factors, including genetics. Differences in taste perception have also been shown to associate with the expression of taste receptor genes, which have not been explored for sweet taste. This study examines the relationship between the sweetness of sucrose (Suc), Acesulfame potassium (AceK), and Rebaudioside A (RebA) and the mRNA expression of TAS1R2, a gene in the sweet taste receptor complex. Initially, 121 participants rated the sweetness intensity of five concentrations of each sweetener. Fungiform papillae were collected, and the relative expression of TAS1R2 was determined using quantitative RT-PCR. After excluding the participants with low-quality data (misuse of the rating scale or amplification below threshold), 40 participants were categorized into 3 groups based on sweetness intensity for each sweetener (Suc, AceK, RebA, respectively): low (n=4; 6; 6), medium (n=18;18; 23), and high (n=18; 16; 11). Results show that mRNA expression of TAS1R2 in human fungiform papillae is significantly associated with the 3 intensity groups for Suc and AceK ($p<0.05$). The low group demonstrated substantially lower TAS1R2 than the medium and high groups. The medium group also showed lower expression levels than the high group, except for AceK. As for Reb A, no significant differences were observed (p=0.74). This study is the first to report on the relationship between the expression of TAS1R2 and the sweetness of both caloric and non-caloric sweeteners. Findings suggest there may be differing mechanisms regulating sweetness perception for RebA compared to Suc and AceK. Further research examining intake may provide new insights into the regulation of TAS1R2 and improve the understanding of the mechanisms regulating taste perception.

350 **Molecular Interactions Between Glutathione And Umami Taste Receptor Tas1R1/Tas1R3**

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Glutathione (γ-L-glutamyl-L-cysteinyl-glycine, GSH) is known for its kokumi properties, able to confer mouthfullness, richness, complexity and intensity to umami, salty, and sweet taste perception. In addition to activating the calcium-sensing receptor, GSH has also been shown to activate the heterodimeric G-protein coupled receptor, TAS1R1/TAS1R3. The TAS1R1 and TAS1R3 subunits are characterized by a large extracellular N-terminal domain, composed of the Venus Fly Trap (VFT) domain followed by a cysteine-rich domain (CRD), which connects to the transmembrane domain (TMD). Previous studies combining molecular docking and site-directed mutagenesis studies combined to cellular assays have shown that l-Glutamate (L-Glu) and 5'-inosine monophosphate (IMP) interact within the VFT of TAS1R1. This stabilizes the closed state and drives the synergism between L-Glu and IMP. In this study we investigated the GSH binding site in the TAS1R1/TAS1R3 receptor and demonstrated its synergism with L-Glu. Using molecular docking, we identified key amino acid residues involved in GSH binding. We further validate the role of these amino acids on GSH-induced activation or synergism by performing cell-based functional assays using human HEK293T cells expressing point mutants of the TAS1R1/TAS1R3 receptor. Cellular responses were measured using a fluorescent protein calcium biosensor after cell stimulation with umami molecules using an automated fluorometric imaging plate reader. Our results demonstrate that GSH interacts at a binding site overlapping with those of L-Glu and IMP within the VFT of TAS1R1.

352 **The Role Of Carbonic Anhydrase Vi (Ca6) In Bitter Taste Perception**

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Salivary proteins (SPs) appear to play a role in bitter taste perception. Our lab has demonstrated in a taste reactivity (TR) paradigm, that rats infused with salivary proteins while they are receiving a quinine stimulus show fewer aversive responses compared to those infused with quinine and saliva that has no proteins present. However, the specific proteins contributing to changes in taste responding remain unidentified. Carbonic anhydrase VI (CA6), a secretory isozyme that is expressed in salivary glands and secreted into the saliva, has been thought to aid in bitter taste perception. To test the role of CA6 in taste responding we delivered recombinantly produced and purified CA6 to rats in the taste reactivity paradigm with and without quinine. We found that when 1mM quinine was administered with CA6, there were less aversive responses than when administering quinine alone. There were no differences in the amount of ingestive responses when administering quinine with or without CA6. Our data suggest that CA6 may be decreasing the bitterness of the stimulus. These findings are in contrast to findings from KO studies. Car6 KO mice appear to increase acceptance for 3μM quinine (Patrikainen et al., 2014). It is currently unclear if the differences between the studies are due to concentration differences, methodological differences, or if the potential role for CA6 in taste bud health (Henkin et al., 1999; Melis et al., 2013) may have played a role in the KO.

354 **Variability Of Olfactory Coding In Ventral Ca1 Region Of The Hippocampus**

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While the ventral CA1 region of the hippocampus (vCA1) has historically been associated with memory, navigation, and anxiety, increasing evidence suggests that chemosensory stimuli may influence vCA1 neural responses. The olfactory cortex sends direct projections to vCA1 and vCA1 sends monosynaptic feedback projections to the granule cell layer of the main olfactory bulb. Despite this reciprocal connectivity and the increasing evidence for use of olfaction in hippocampal-related behaviors, vCA1's role in encoding and processing olfactory stimuli remains poorly understood. A necessary first step toward resolving this question to is to identify whether features of olfactory stimuli such as odorant identity are encoded for in the firing of neurons in vCA1. To address this, we performed high-density extracellular electrophysiology recordings in vCA1 in awake head fixed 2-3-month-old C57BL/6J female mice (n = 4) as they ran on a wheel while passively exposed to volatile monomolecular odorants. When we examined neural activity in vCA1 (n = 33 single units), we found 55% of units exhibited odorant tuning. For comparison, the estimate of place cells in the literature in vCA1 is around 10-20%. Odorant tuned units were responsive to anywhere between one and three odorants out of the ten-odorant panel, and both excitatory and inhibitory responses were observed. Furthermore, responses were observed across the population to several classes of odorants as defined by chemical functional groups. Understanding olfactory representations in healthy ventral hippocampal circuits will lay the groundwork for

studying the role that changes in hippocampal circuitry may play in mediating co-occuring changes in cognition, emotional regulation, and olfactory perception seen in neurodegenerative diseases.

356 **Locomotion Modulation Of Neural Representations Of Odors In The Rodent Main Olfactory Bulb**

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Olfactory behaviors like navigating towards an odor source or tracking an odor trail (Khan et al 2012) require locomotion; this movement both assists in the tracking of chemosensory cues (Findley et al, 2021) but also alters those cues due to self-generated motion. While odors are encoded through spatiotemporal patterns of activity across populations of mitral and tufted (M/T) cells in the main olfactory bulb (MOB), recent work has demonstrated that M/T cells are also capable of encoding locomotor information, independent of odor encoding (Chockanathan et al, 2021). This adds to an existing body of literature demonstrating that M/T cell activity and responses to odors can be modulated by behavior (Kay and Laurent, 1999). An open question is thus how M/T cell encoding of behavior shapes the stability and variability of the neural responses to odors. To address this question, we performed high-density recordings of M/T cell responses to an array of monomolecular odors (N=22 odors) in the MOB of awake head fixed mice (N=6) on a running wheel. In tandem, we monitored other aspects of behavior such as the animal's sniffing, which is affected by running, and has a strong modulatory effect on the precise timing of neural activity in response to odor presentation. We found that both single neuron and population responses to odors were variable across different time scales due to behavior. While some neurons encoded odors independently of the locomotor behavior, other cells showed significant modulation of trial-to-trial responses to the same odor in neural activity due to locomotion. Thus, odor encoding by M/T cells in the bulb requires consideration of not only the identity or concentration of those odors, but also the locomotor behavioral state of the animal.

358 **Utilizing Olfactory Receptor-Defined Glomeruli To Investigate The Organization Of Inhibition In The Mammalian Olfactory Bulb.**

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In the early olfactory system, the functional organization of inhibitory circuits remains unclear, partly due to challenges in mapping receptor-level responses to principal output neurons and characterizing responses of the same glomeruli across individuals. To address this, we generated three odorant receptor (OR)-tagged mouse lines in which OSNs expressing a given OR also express mKate2. The lines targeted one class I (Or52h2) and two class II ORs (Or10g9b and Or1ad1), and each was crossed with mice expressing genetically encoded calcium reporters in MT cells or OSNs. We probed OR-tagged glomeruli with large odorant panels (40-50) in awake mice to characterize pre- and post-synaptic excitatory and suppressive tuning. We tested two models of lateral inhibition between glomeruli: a nonuniform/random model, predicting variability in odors suppressing a given glomerulus across individuals, and receptor-defined, predicting stereotypy of suppressive responses relative to odor and receptor identity. The suppressive response spectrum of Or52h2 MT cells showed evidence of both feed-forward inhibition (associated with weak OSN excitation) and lateral inhibition (suppressive responses in the absence of OSN excitation). Notably, odorant-driven suppressive responses were stereotyped within and across individuals, supporting the receptor-defined model of lateral inhibition. In addition, lateral inhibitory connections appeared domain-specific, as class II OSN-activating odorants did not suppress Or52h2 MT cells. Interestingly, odorant-evoked suppression was less prevalent in the MT cells of the class II (Or1ad1 and Or10g9b) glomeruli. These results suggest that lateral inhibition in the olfactory bulb is selective, targeted to specific receptor-defined glomeruli, and heterogeneous across different OR classes.

360 **The Neural Signature Of Perceived Odor Intensity**

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Olfaction is a cardinal sense for most animal species. Behaviors such as foraging and navigation all heavily rely on the ability to interpret odor intensity information. Understanding how the brain encodes odor intensity is vital for gaining insight into how the brain accomplishes odor-guided behaviors. Studies showed that changes in odorant concentration correlate with changes in neuronal firing rate, temporal shifts in response pattern relative to inhalation, or overall synchrony of neural responses. However, odor concentrations are inappropriate proxies

for perceived intensity: at similar concentrations some odors evoke strong sensations, while others are barely perceivable. Therefore, it remains unclear which neural phenomena underlie the perception of odor intensity. One major challenge in studying the neural encoding of intensity is obtaining perceptual reports and neural recordings from the same animal model. Here, we combined mouse and human data to formulate a unified theory of the neural encoding of odor intensity. We used a behavioral paradigm in mice that allowed us to measure iso-intense odorant concentrations. In mice, we computed the iso-intense concentrations for three odor pairs at three concentration ranges. We repeated this paradigm in humans and verified that it accurately predicts panelists' explicit intensity ratings. We then combined these results with calcium imaging in mice and electrophysiology recordings in mice and humans to ask which neural features in the olfactory bulb and piriform cortex predict intensity equivalency at iso-intense concentrations. We propose that odor intensity could be encoded by neural firing synchronization. By combining mouse and human behavior and recordings, we can propose robust hypotheses on the neural encoding of perceived odor intensity.

362 **Predicting Olfactory Mixture Similarity Perception Through A Community Effort**

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A key goal of sensory sciences is to establish the rules linking shifts in physical stimulus structure to predictable shifts in perception. These rules are better defined in vision and audition than in olfaction. Their absence in olfaction hinders the digitization of this sensory domain. The quest to establish such rules includes predicting odorant verbal labels and predicting pairwise stimulus perceptual similarity. A strong framework for perceptual similarity is widely seen as key to labeling stimuli and, ultimately, digitization. The DREAM Olfactory Mixtures Prediction Challenge aimed to highlight models predicting the perceptual similarity of molecular mixture pairs from a curated dataset of multiple studies. This dataset comprises 850 unique mixtures, 235 mono-molecules, and 780 mixture pairs. Teams competed for three months to develop machine-learning models predicting how close two molecular mixtures are in odor perceptual space (0-1 scale, where 0 indicates total overlap, and 1 is furthest apart) using chemical and semantic descriptors. Feedback on the leaderboard dataset of 46 mixture-pair comparisons helped refine models and compare performance. Final predictions were made on a hidden test set of 46 comparisons. DREAM organizers evaluated models using 10,000 bootstrap iterations, with RMSE and Pearson correlations as metrics. The competition ended in a quadruple tie. We built an ensemble model from the top 8 teams' predictions, which outperformed all individual models with an RMSE of 0.08 and Pearson correlation of 0.6. This ensemble model surpassed state-of-the-art models, including Snitz Angle, Principal Odor Map, Semantic, and Pair models. These rules may enable smell digitization, with further improvements expected from larger datasets.

364 **1,1,6-Trimethyl-1,2-Dihydroxnapthalene (Tdn) Is A Common Odor Defect Of Riesling Wine (Petrol) That Screams &Ldquo;Riesling&Rdquo; At Subthreshold Levels.**

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The idiosyncratic odor character of white wines, caused by their viticulture, enology, and aging, is a consequence of the ratios of a small subset of Key odorants. Riesling shares these key odorants with many white wines while maintaining its unique identity. 1,1,6-Trimethyl-1,2-dihydroxnapthalene (TDN), a unique odor defect in Riesling has a 'petrol' note when present above its threshold but it is found near its threshold in most Rieslings. In rat neurobiology, a "silent note" is a nonlinear response that creates mixture identity (Xu and Firestein 2021). We have investigated the role of TDN concentration in the recognition of Riesling character as a "silent note". We presented Riesling-familiar subjects with 75ms duration puffs of 10mL Chardonnay headspace containing different ratios of TDN and measured their response to the binary forced-choice: "Riesling" or "not Riesling". The response probability was fit to logistic models of response probability vs molar concentration of TDN in the Chardonnay. Separately, Riesling-familiar subjects were stimulated with the same Chardonnay-TDN samples but were asked "petrol" or "not-petrol". These results were fit to a logistic model, with the predicted 0.5 probability of recognizing "petrol" defined as the threshold for TDN in Chardonnay. The subjects had similar but unique thresholds for TDN perceived as "petrol" in Chardonnay wine, but all subjects responded positively to recognition of "Riesling" odor at concentrations of TDN below the threshold for TDN in Chardonnay. At super-threshold levels, TDN in Chardonnay is recognized as "petrol", a defect of Riesling. At sub-threshold levels in Chardonnay, TDN creates a "silent note" that screams Riesling.

366 **Estimating Perceived Odor Intensity In Mice**

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Intensity is a key property of sensory processing that is critical for animal behaviors such as navigation and foraging, but how odor intensity information is processed by the brain to perform these behaviors is still

unknown. Studies have highlighted the existence of several neural correlates of odorant concentration, however, concentration is an inaccurate descriptor of perceived intensity. Indeed, the relationship between concentration and intensity is complex and odor-dependent: the same concentration of different odorants can evoke dramatically different perceptual experiences. Hence, understanding the neural processing of perceived odor intensity hinges on the possibility of obtaining neural recordings and perceptual reports in the same model system. Here, we developed a behavioral paradigm to measure perceived odor intensity in mice. We first used this paradigm to measure which concentrations of odor pairs are perceived as iso-intense by mice. This was repeated for three odor pairs at three different concentration ranges (low, medium, and high). We then used sigmoidal functions to model the relationship between concentration and perceived intensity, and wrote equivalency equations for a subset of the iso-intense concentrations. Using these equations as constraints, we employed a differential evolution optimization algorithm to estimate the parametric relationship between the concentration and the perceived intensity of each odorant. The concentration-intensity curves successfully predicted held-out iso-intense concentrations for the three odor pairs (RMSE = 0.021±0.018 mean and s.d). Our results show a novel and reliable method to measure perceived odor intensity in mice. We will leverage these results to ask which neural activity features are critical to encoding perceived odor intensity.

368 **Order Code In The Olfactory Bulb**

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What is the structure of odor representations formed by the olfactory system? In this study, we analyzed glomerular responses in the mouse olfactory bulb to large sets of odorants obtained using calcium imaging. The primacy model suggests that odor identity is encoded by high-affinity sets of olfactory receptors (ORs) called primacy sets. According to this model, ORs that do not belong to any primacy set (null ORs) are eliminated during evolution. The remaining ORs form a low-dimensional structure known as the primacy hull. To test this hypothesis, we embedded recorded OR/glomerular responses into a receptor space using multidimensional scaling (MDS). We found that in the receptor space, ORs/glomeruli form two clusters with distinct odor-tuning properties. The clusters create two independent primacy sets for individual odors, contributing to two distinguishable primacy hulls for odor ensembles. Notably, the OR clusters contain few null ORs (non-primary to any odor), compared to a randomly shuffled dataset, as predicted by the primacy theory. OR activation in response to odors occurs in temporal waves that show orderly patterns in the receptor space. The waves' directions do not align across the two OR clusters. The directions of OR recruitment waves are determined by the odorants and can be used to represent odor identity. Odor representations based on OR recruitment wave directions are consistent across individual animals and allow us to build an accurate cross-animal and cross-concentration odor identity classifier. Together, these findings suggest that ORs form two separate encoding channels, each with its own primacy receptor set (primacy hull). We propose that the order of OR activations generates a robust odor representation that generalizes well across different animals and concentrations.

370 **Dream Olfaction Challenge Iii: Prediction Odor Quality Perception Of Mixtures**

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The mapping of physical properties to perception is well-established in vision and audition; however, our understanding of olfaction, particularly the link between structure and percept, lags far behind. Recent advances in predictive models and additional perceptual data have enabled models to predict odor perceptions from molecular structures for pure odorants. However, extending these models to accurately predict the perception of realistic olfactory mixtures remains a significant challenge. The second DREAM olfaction challenge developed models to predict the discriminability of olfactory mixtures, achieving an ensemble model performance of root mean square error (RMSE) 0.08 and Pearson correlation 0.6, while highlighting the need for larger datasets and refined approaches to address the complexities of olfactory perception. Building on this foundation, a third DREAM olfaction challenge aims to advance the field by focusing on predicting the perceptual characteristics of olfactory mixtures, addressing broader aspects of human olfactory perception beyond discriminability. This year the challenge will feature a larger unpublished mixture dataset with detailed odor profiles for over 700 mixtures. These mixtures are composed of 2, 3, 5, or 10 components from a pool of over 150 monomolecular odors. The odors of every component and mixture were described by at least 15 trained panelists using the rate-all-that-apply (RATA) method and a 51-word odor lexicon. During training sessions, each term in the lexicon was paired with visual and odor references. Through this larger dataset and challenge framework we hope to identify new models that allow us to predict how humans perceive realistic mixtures.

372 **Assessing The Chemosensory Tuning Of Mouse Accessory Olfactory Bulb Mitral Cells Across Sexes, Stimulus Concentrations, And Cellular Compartments**

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The accessory olfactory system (AOS) in most mammals detects social chemosignals from body fluids like urine and regulates behaviors such as mating and aggression. These social cues are detected in the vomeronasal organ

(VNO), which transmits chemosensory information downstream to the accessory olfactory bulb (AOB). There, mitral cells (MCs) further process this information and through their activity patterns influence multiple behaviorally important circuits. Significant gaps remain in understanding of MC function, including how they organize their activity patterns in response to conspecific cues across concentrations. We lack a complete understanding of how other factors affect MC tuning, including sex, age, and past chemosensory experience. Additionally, it remains unclear how AOB mitral cells' anatomy, which differs from mitral cells in the main olfactory bulb, contributes to their chemosensory tuning. To address these gaps, we measured MC calcium responses to a panel of natural stimuli using an AOS *ex-vivo* preparation that preserves the connectivity between the VNO and the AOB. Using a customized 2-photon imaging setup, we imaged virally-mediated GCaMP6f fluorescence in AOB MCs from adult male and female *Pcdh21-cre* transgenic mice while we stimulated the VNO with a panel of conspecific urine stimuli across multiple concentrations. We compared the responses of AOB MCs in various cellular compartments, including glomerular tufts, primary dendritic branches, and somas. These data inform our fundamental understanding of AOB function, and provide a basis for future studies relating prior experience to neuroplasticity and behavioral modulation in this important social chemosensory pathway.

374 **The Natural Statistics Of Human Olfactory Experience: A Multi-National Project**

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How many distinct odors does a typical human encounter throughout a typical day, and what are these odors? What are the sources of variance underlying this question? How different is the answer for different people in the same place and time, or for people across places and times? We have a very poor grasp on the natural statistics of the human olfactory experience. To probe this, in a multi-national ERC-supported project we built a cellphone app that probes the user at random times to report on their olfactory experience. Two questions: "Do you currently smell anything?" and "Were you aware of the odor before we asked?" are followed by a series of rating scales, and an option to photograph the odor source. From 28 out of an intended 24,000 participants, our data suggests odorant presence at about 50% of waking time, but awareness for the odor at 30% of time, with highest prevalence between 14:00 – 15:00 and 18:00 – 19:00. The most reported smell was "Coffee" (52 reports) followed by "Food" (36 reports) and "Perfume" (21 reports). We have only started to disseminate the app, and expect data from 1 million entries to answer the questions posed at the outset of this abstract.

376 **Hanvonvs: A Machine Learning Framework For Efficient And Accurate Prediction Of Olfactory Receptor-Odorant Interactions**

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The binding of olfactory receptors (ORs) to odorants is a fundamental mechanism underlying the perception of external odors in vertebrates. Current olfactory research relies heavily on *in vitro* experiments, which are time-consuming and resource-intensive. Recent advancements in machine learning-based virtual screening methods in conjunction with the exploration of relationships between odorants and ORs have spurred significant interests in the field of artificial intelligence. In this study, HanvonVS was developed as a sequence-based virtual screening model to predict OR-odorant binding probability and affinity. The model integrates multidimensional features, including evolutionary information, physicochemical properties, conformational data, and functional annotations to comprehensively represent the interactions between ORs and odorants. By combining Graph Neural Network (GNN) with olfactory-specific feature selection and a graph clustering approach guided by chemical bond constraints, HanvonVS effectively captures complex relationships and achieves precise predictions of OR-odorant interactions. A dataset of approximately 150,000 experimental records, detailing interactions between 2,072 ORs (variants) and 834 odorants, was used for training. To further evaluate its predictive capabilities, additional odorants outside the training dataset were tested. The predictions of the model were confirmed experimentally, showing a reasonable alignment with the results. HanvonVS has the potential to revolutionize olfactory research by improving experimental efficiency and enrichment. It provides valuable insights into binding mechanisms and serves as a powerful tool for exploring the science of olfaction while unlocking practical applications in related fields.

378 **Diff-Sense: A Deep Learning-Based Diffusion Model For Predicting Olfactory Receptor-Odorant Interactions Through Multilevel Feature Fusion**

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Olfaction, a critical sensory function in mammals, is primarily triggered by the specific recognition and binding of odorants by olfactory receptors (ORs) in the nasal mucosa, ultimately leading to the perception of smell. However, the prediction of the interaction between odorants and ORs is still challenging due to the enormous diversity and discontinuous nature of the olfactory perception space. In this study, we present Diff-Sense, a diffusion generative model that employs Special Euclidean group in 3D (SE3) to construct the interaction of

odor-receptor, promoting efficient transitions between different equilibrium states. In Diff-Sense, multi-level feature fusion (MFF) is employed to extract comprehensive information from odorants, including spatial characteristics, functional groups, and physicochemical properties. MFF is consisted of a two-stage approach: (1) Molecule-Atom Fusion Network (MAN) captures atomic properties, molecular fingerprints, molecular properties and 3D structural information of an atom or molecule. (2) Reduced Molecular Graphs Fusion (RMG) obtains the pharmacophore and the functional group to refine molecular representation via combination of reduced molecular graphs. Our findings demonstrate that MFF effectively reduces the prediction error caused by the insufficiency of information on odorants and experimental solved ORs with a 46.67% accuracy (ligand RMSD <2Å). Furthermore, Diff-Sense facilitates the identification of binding modes between all human olfactory receptors and a majority of key food odorants, promoting the understanding of the molecular recognition mechanisms underlying odor perception in the olfactory system. Diff-Sense is constructed to support the research of olfactory mechanisms, the diagnosis and treatment of olfactory dysfunctions, and the development and optimization of flavors and fragrances.

380 **Olfactory Aversive Conditioning And Detection Of Target Odors In Drosophila Melanogaster**

Lautaro Duarte[1], Martín Klappenbach[1,2], Nicolás Pírez[1,2], Fernando Locatelli[1,2]

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Odorants are detected by olfactory receptor neurons (ORNs) that project to the antennal lobe (AL), the first olfactory neuropil in the insect brain. In the AL, ORNs make synaptic contacts with: i) projection neurons (PNs), which in turn send olfactory information to other brain areas; and ii) local interneurons (LNs) that form a dense network of lateral inhibitory and excitatory interactions within the AL. Functional and computational studies indicate that this local network transforms sensory input, presumably to enhance perception of meaningful odors. Here, we investigate the role of GABAergic local neurons in both learning-dependent plasticity in the AL and the ability of flies to perceive the presence of learned odorants in a mixture. For that aim, we performed aversive olfactory conditioning using a single odorant as a conditioned stimulus. Next we tested olfactory avoidance in a T-maze by exposing the flies to the conditioned odorant by itself, or in a mixture of different proportions with a novel odorant. We determined the threshold proportions that flies need to detect the learned odorant immersed in the mixture. These proportions are odorant and mixture specific. Next, we studied whether blocking the activity of different groups of LNs in the AL modifies the animals ability to detect learned odorants embedded in mixtures. Finally, we asked wheater olfactory aversive conditioning affects the representation of odorant mixtures in the AL. We recorded odorant evoked responses of PNs using calcium imaging, while concomitantly training animals with the same protocol used in the T-maze experiments. By using this experimental set up we were able to study odorant representation before and after training, and found that the representation of a binary mixture in the AL changes after aversive learning.

382 **An Overview Of Human Odorant Receptors And Their Identified Agonists**

Maxence Lalis[1], Matej Hladiš[1], Loïc Briand[2], Sébastien Fiorucci[1], Jérémie Topin[1]

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Olfactory perception occurs when odorous molecules activate specialized sensory receptors on neurons. Smell recognition relies on a combinatorial activation code of odorant receptors (ORs), though the rules governing ligand recognition remain poorly understood. Focusing on the cornerstone of smell perception, the olfactory receptors (ORs), we introduce M2OR[1], a database featuring 75,050 experimental measurements across 1,257 OR sequences from 11 species. This database is carefully curated to ensure accurate molecular representation, including the differentiation of isomers essential for olfactory recognition. It also provides detailed information on biological assays, such as cell lines, readout methods, and G-protein types. An analysis of OR-molecule interactions reveals that 83% of results are consistent across experimental conditions, with most ligands exhibiting micromolar activity. For human ORs, 88% remain to be deorphanized. Additionally, the study estimates OR recognition range and proposes a framework for comparing future machine learning models predicting OR-odorant interactions[2]. [1] M. Lalis, M. Hladiš, S. A. Khalil, L. Briand, S. Fiorucci, J. Topin. M2OR: a database of olfactory receptor–odorant pairs for understanding the molecular mechanisms of olfaction, *Nucleic Acids Research*, 2024, https://doi.org/10.1093/nar/gkad886. [2] M. Lalis, M. Hladiš, S. A. Khalil, C. Deroo, C. Marin, M. Bensafi, N. Baldovini, L. Briand, S. Fiorucci, J. Topin*. A status report on human odorant receptors and their allocated agonists, *Chemical Senses* 49, 2025 : bjae037.

384 **Neural Responses In The Anterior Piriform Cortex Of Freely Moving Mice To Non-Social And Social Odors**

Ryan C. Scauzillo, Max L. Fletcher
University of Tennessee Health Science Center, Memphis, TN, United States

As animals traverse habitats, they are inundated with various odors that they must differentiate in order to engage in proper behavior such as foraging, threat response, or social. Within the main olfactory circuit, the piriform cortex is the primary center for odor coding showing responses to various odors including social and non-social odors. While the main olfactory system is not considered to be the main processing center for olfactory driven social behavior, we believe that is it still an integral part likely working in conjunction with the accessory olfactory system. We thus hypothesize that within the anterior piriform cortex there will be differential responses to social versus non-social odors. To test this, we utilized head-mounted miniscopes to record neural activity of freely moving mice investigating social and non-social odors. Mice were placed in a rectangular arena that

contained a port for the presentation of odors. Mice were presented with 10 different odors for a minimum of 30 seconds or until the odor was investigated. Neural responses in the anterior piriform cortex were generally stronger to social odors compared to non-social odors for both male and female mice. Similarly, the percentage of responding neurons was generally greater for social odors compared to non-social odors for both male and female mice. The neural responses to social odors in the main olfactory circuit may indicate parallel processing that works in conjunctions with the accessory olfactory system.

386 **Context Dependent Odor Processing In The Human Brain**

Qiaohan Yang, Naelly Arriaga, Vivek Sagar, Guangyu Zhou, Andrew Sheriff, Gregory Lane, Nathan Anderson, Rodrigo M. Braga, Christina Zelano
Department of Neurology, Feinberg School of Medicine, Northwestern University, Chicago, IL, United States

Context-dependent flexibility in odor object coding is a fundamental aspect of human odor processing. Odor stimuli encountered daily can often be ambiguous, which requires the human brain to analyze not just the perceptual features, but also the context in which these odors are received (their source) to distinguish odor objects and guide decisions. Humans regularly make approach/avoidance decisions about odors based on contextual cues. For example, the cheese-like smell of valeric acid may smell appealing when emanating from cheese, but may be aversive from a person. The human primary olfactory cortex is comprised of multiple cortical regions, each receiving monosynaptic input from the olfactory bulb in a parallel fashion. These include the anterior olfactory nucleus, olfactory tubercle, piriform cortex, parts of amygdala (the medial amygdala, anterior cortical amygdala, and the pariamygdaloid complex), and entorhinal cortex. How the system achieves context-dependent coding flexibility and guides our decisions is unknown. It is hypothesized that the parallel organization of the olfactory system may facilitate the extraction of information under different contexts. Using high-resolution fMRI, we will investigate how context-dependent coding is realized in the human olfactory system. Preliminary behavioral analyses confirmed that context modulates approachability of identical odor stimuli. Further analyses will investigate the neural underpinnings of contextual coding in the human olfactory system.

10:00 - 12:00 PM	Calusa EFGH
In Vivo Visualization of the Human Olfactory System	

Chair(s): Eric Holbrook

Advancing Techniques Toward In Vivo Visualization Of The Human Olfactory System.
Eric H. Holbrook
Harvard Medical School Massachusetts Eye and Ear, Boston, MA, United States

Advancements in optics and imaging techniques push the boundaries to what we are able to observe on both a microscopic and macroscopic scale in the olfactory system. However, our ability to visualize human peripheral and central olfactory components in detail and in real time is grossly deficient. This greatly limits our ability to observe systemwide changes related to damage and pathologic disease or the extent of recovery during regeneration. This symposium brings together researchers in fields of olfaction as well as imaging technology with a focus on the possibility for future in vivo olfactory imaging that will allow for real-time observation of the peripheral and central olfactory system in humans.

Potential Methods For In Vivo Imaging Of Human Olfactory Tissue.
Eric H. Holbrook[1,2], Hironobu Nishijima[2,3], James E. Schwob[2], Brian Lin[2], Anastasia Yendiki[4], Ting Gong[4]
[1]Harvard Medical School, Massachusetts Eye and Ear, Boston, MA, United States, [2]Tufts University School of Medicine, Boston, MA, United States, [3]The University of Tokyo, Tokyo, Japan, [4]Harvard Medical School, Massachusetts General Hospital, Boston, MA, United States

Although advances in techniques for visualizing the olfactory pathways at a micro and macro level has progressed, challenges remain in imaging olfactory structures in vivo. This dearth of ability becomes even more apparent when considering evaluation of human olfactory disorders. The field requires methods for observing peripheral and central anatomy in conditions of olfactory loss that can be administered both repeatedly and in a safe manner to allow for monitoring of incremental changes without disruption. We present two techniques with the potential for dynamic monitoring of human olfactory changes: 1) using topically applied nasal compounds that rely on differential expression of epithelial based enzymes for fluorescent activation and labeling, and 2) through diffusion MRI based imaging of the peripheral and central olfactory pathways. A discussion will outline the limitations and challenges of these techniques and the need for further development. The importance for developing methods for visualizing and assessing changes in the olfactory pathway during olfactory loss as well as recovery will be stressed.

Imaging The Nasal And Olfactory Epithelium With *In Vivo* Microscopy
Hinnerk Schulz-Hildebrandt[1], Brian Lin[2], Erica Villareyna Lopex[1], Eric H. Holbrook[4], Guillermo J. Tearney[1]
[1]Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States, [2]Tufts University, School of Medicine, Boston, MA, United States, [3]Wellman Center for Photomedicine, Massachusetts General Hospital, Boston, MA, United States, [4]Harvard Medical School Massachusetts Eye and Ear, Boston, MA, United States

In the study of the respiratory and olfactory epithelium within the nose, optical coherence tomography (OCT) has proven to be an invaluable tool for visualizing tissue structures. However, traditional OCT lacks the resolution necessary to resolve individual cells, limiting its application in cellular-level imaging of physiological processes such as ciliary movement and mucus secretion. To address this limitation, our lab has developed micro-optical coherence tomography (μOCT), which offers 1 μm resolution and captures up to 150 frames per second. This enhanced imaging capability enables us to visualize the nasal and olfactory epithelium in greater detail, providing real-time insights into mucus transport and secretion. Despite these advances, differentiating between nasal and olfactory epithelial cells remains a challenge. In this presentation, we will demonstrate how dynamic μOCT leverages temporal signal fluctuations, originating from cellular metabolism, as a novel contrast mechanism. This approach allows us to study both physiological and pathological processes in the nasal and olfactory epithelium. We believe this technique has the potential to deepen our understanding of the dynamic interactions within the nasal and olfactory epithelium and how they respond to disease.

Non-Invasive Method To Measure Olfaction And Smell Disorders Using Flourescene Agent Targeting Nav1.7
Dauren Adilbay [1,2,3], Junior Gonzales[1], Marianna Zazhytska[4], Paula Demetrio de Souza Franca[1,5], Raik Artschwager[1], Snehal Patel[2], Albana Kodra[4,6], Jonathan Overdevest[7], Chun Yen Chow[8,9], Glenn King[8,9], Sanjay Jain[10,11], Alvaro Ordonez[10,11], Laurence Carroll[10,11], Stavros Lomvardas[4], Thomas Reiner[1,12], Naga Vara Kishore Pillarsetty[1,12]
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United States, [5]Department of Otorhinolaryngology and Head and Neck Surgery, Federal University of São Paul, Sao Paulo, Brazil, [6]Department of Genetics and Development, Columbia University Irving Medical Center, Vagelos College of Physicians and Surgeons, Columbia University,, New York, NY, United States, [7]Department of Otolaryngology-Head and Neck Surgery, Columbia University Irving Medical Center, Vagelos College of Physicians and Surgeons, Columbia University, , New York, NY, United States, [8]Institute for Molecular Bioscience, University of Queensland, St. Lucia, Australia, [9]Australian Research Council Centre of Excellence for Innovations in Peptide and Protein Science, University of Queensland,, St. Lucia, Australia, [10]Center for Infection and Inflammation Imaging Research, Johns Hopkins University School of Medicine,, Baltimore, MD, United States, [11]Russell H. Morgan Department of Radiology and Radiological Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, United States, [12]Department of Radiology, Weill Cornell Medicine, New York, NY, United States

Objective: Currently there are no objective methods to measure loss of olfaction. Voltage gated sodium channel 1.7 ($Na_V1.7$) is the predominant sodium channel in olfactory sensory neurons (OSN) that plays major role in olfaction. Tsp1a is a natural peptide derived from spider toxin that targets $Na_V1.7$ with high selectivity. In this study, we examined whether $Na_V1.7$ expression is associated with olfaction and whether signal from fluorescently labeled Tsp1a could function as a readout for olfactory function. Methods: Athymic nude mice were intravenously (i.v.) injected with Tsp1a-IR800 and epifluorescence images were acquired using an IVIS Spectrum animal imaging system and average radiant efficiency in the region of the olfactory epithelium/bulb (ROEB) was measured. Methimazole was used to chemically ablate the olfactory epithelium in mice. Buried food test as performed to measure time to find food and correlate with fluorescence signal. Immunoshistochemistry (IHC), Single cell RNA sequencing(scRNA-seq) and bulk RNA-seq was performed on olfactory epithelium of SARS-CoV-2 infected mice and hamsters and human cadavers. Results: The area of ROEB was clearly visible in epifluorescence *in vivo* images of mice and significant reduction in signal was observed after olfactory ablation. Inverse correlation between the time to find buried food and radiant efficiency. Mice after olfactory ablation as well as SARS-CoV-2 infection had significantly lower expression of $Na_V1.7$. RNA-seq from hamsters ROEB tissues and humans OSN cells revealed significantly lower level of SCN1A gene RNA expression post SARS-CoV-2 infection. Conclusion: We demonstrate fluorescent imaging of mouse epithelium is possible, suggesting that labeled Tsp1a tracers may serve as an objective diagnostic tool for loss of smell.

Polak Young Investigator Awardee: High-Speed Volumetric Imaging Of The Olfactory System: From Periphery To Cortex

Lu Xu[1], Wenze Li[1], Eliza C. B. Jeager[2], Nicholas J. Chua[2], Stuart J. Firestein[2], Elizabeth M. C. Hillman[1,2], Maria A. Tosches[2]

[1]St. Jude Children's Research Hospital, Memphis, TN, United States, [2]Columbia University, New York, NY, United States

Swept Confocally-Aligned Planar Excitation (SCAPE) microscopy is a light-sheet-based volumetric imaging technique that enables high-speed, high-resolution 3D imaging of biological samples. Light-sheet illumination provides reduced photodamage compared to confocal microscopy, while SCAPE's unique single-objective design significantly reduces the spatial constraints of light-sheet microscopy, enabling imaging of diverse intact and in-vivo samples. We have leveraged these benefits of SCAPE microscopy, combined with fluorescent calcium indicators to study the olfactory system across species. First, we recorded activity from tens of thousands of olfactory sensory neurons simultaneously in the mouse olfactory epithelium in an intact *in vitro* preparation, revealing a receptor-driven modulation effect that shapes coding of mixtures of odors at the peripheral level. More recently, we have leveraged SCAPE microscopy to capture large-scale, odor-evoked neuronal activity in the intact brains of behaving salamanders, while simultaneously resolving the 3D morphology of individual neurons. Together with our custom analysis pipelines, SCAPE microscopy provides a powerful tool for studying olfactory coding across peripheral and central circuits in real time and at large scale. This approach holds broad potential for investigating other dynamic biological processes in diverse samples.

Development Of A Multiphoton Endoscope For Clinical Imaging Of Human Olfactory Epithelium

Emily A. Gibson[1], Diego Restrepo[2], Skylar Suarez[1], Conner Massey[3]

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Multiphoton microscopy is a widely used technique in biomedical research due to its high spatial resolution and ability to image cellular-level functional information in a non-invasive manner. Multiphoton microscopy encompasses a variety of different optical modalities including second- and third- harmonic generation, two-photon fluorescence, and coherent Raman scattering microscopy. Each modality can provide image contrast for different structural and functional features in unlabeled tissue. I will discuss current research progress in developing a microendoscope for multiphoton imaging of the olfactory epithelium and future directions for clinical applications.

10:00 - 12:00 PM	Calusa ABC
Where the olfactory and reward system meet	

Chair(s): Wolfgang Kelsch and Sarah Sniffen

Invited Symposium: Encoding Odor Value - Where The Olfactory And Reward System Meet

Wolfgang Kelsch[2,3], Sarah Sniffen[1]

[1]Departments of Neuroscience and Pharmacology & Therapeutics, Florida Chemical Senses Institute, University of Florida College of Medicine, Gainesville, FL, United States, [2]Central Institute of Mental Health, Heidelberg University, Mannheim, Germany, [3]Johannes-Gutenberg University Mainz, Mainz, Germany

How do odors acquire value? The answer to this question lies in brain regions that integrate olfactory information and hedonic value. The olfactory tubercle, also known as the tubular striatum, was originally classified as an olfactory cortical structure with direct input from the olfactory bulb. However, over the last decade, exciting progress has advanced our understanding of the tubercle as a key region of the mesolimbic system integrating chemosensory information into value processing. These discoveries have inspired this first AChemS symposium dedicated to the olfactory tubercle. This symposium will address i) new insight into the tubercle's role in the coding of both odor identity and odor value, ii) its involvement in hedonic processing in rodents and humans, and iii) the neural circuits underlying its influence on behavior. Overall, these findings emphasize the special role of the olfactory tubercle in the integration of both odor identity and hedonic value and position it as a central hub for orchestrating odor-driven behavior.

Impact Of Early Life Adversity On Hedonic Odor Perception: The Role Of The Olfactory Tubercle

Anna Athanassi[1], Laura Chalençon[1], Louis Foucault[2], Olivier Raineteau[2], Cecilia Neige[3,4], Laetitia Imbert[3,4], Maylis Duma[3,4], Jérôme Brunelin[3,4], Kevin Bath[5,6], Nathalie Mandairon[1]

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Early life adversity (ELA) such as childhood maltreatment can predispose individuals to adult depression by profoundly altering the development of neural circuits involved in emotional regulation. Depression often manifests alongside disruptions in olfactory hedonic perception, crucial for both vital behaviors and good quality of life. Disruptions in olfactory function can diminish daily pleasures, exacerbating the development and severity of depressive pathology. Understanding the mechanisms underlying ELA-induced olfactory alterations is therefore crucial for developing effective therapeutic strategies aimed at improving the quality of life for individuals who have experienced ELA. In this context, using a mouse model of ELA, we found that ELA reduced the investigation of pleasant odorants and altered the morphology of neurons in the olfactory bulb that are specifically responsive to pleasant odorants. This resulted in disrupted neural processing within the OB and its output message. Furthermore, the olfactory tubercle, a direct target of the OB and a key component of the brain's reward circuitry exhibited altered neural activity in response to pleasant, but not unpleasant, odorants. These alterations were accompanied by altered ventral tegmental area activity that is recruited during approach behavior to pleasant odorants. These results indicate that ELA modifies the neural substrates underlying the perception of pleasant odorants offering insights into the severity of symptoms in individuals at risk of depression with a history of early stress. This study has been extended to humans by studying the influence of ELA on odor hedonics and brain imaging.

A Mesolimbic Channel Shapes Predictive Dopamine Signaling Through Respiratory Coupling

Max Scheller[1,2], Wolfgang Kelsch[1,2]

[1]Department of Psychiatry, Johannes-Gutenberg University, Mainz, Germany, [2]Central Institute of Mental Health, Heidelberg University, Mannheim, Germany

Dopamine neurons encode predicted value of a conditioned stimulus in reinforcement learning. How this value is computed from the inputs of connected brain regions is less clear. To arrive at a more detailed and dynamic description of dopaminergic computation, we studied odor-outcome-associations in the mesolimbic loop. We concurrently recorded the activity of optogenetically identified dopamine neurons in the ventral tegmental area and medium spiny neurons in the olfactory tubercle of the ventral striatum. During these recordings, mice learned an olfactory go/no-go task over weeks. With learning, a characteristic shift emerges in the firing coupled to the sniff phase of dopamine neurons during the inter-trial interval. This emerging inter-trial phase coupling is correlated with the acquired predictive odor stimulus responses. Importantly, sniff coupling of dopamine neurons evolves to a slightly later phase of the sniff cycle than tubercle neurons . Consistent with the phase lag of the two regions, we find an increasing directional coupling of the olfactory tubercle to dopamine neurons with learning. These findings reveal that olfactory conditioning shapes a channel from the olfactory tubercle to midbrain dopamine neurons. This channel carries the predictive value coding with firing activity coupled to the sniff cycle.

These findings highlight the role of the olfactory tubercle as a key hub for olfactory reinforcement learning and a channel connecting olfactory stimuli to dopaminergic prediction coding.

Directing Negative Emotional States Through Amygdala-Striatal Circuitry

Sarah E. Sniffen[1], Sang Eun Ryu[1], Milayna M. Kokoska[1], Janardhan Bhattarai[2], Yingqi Wang[2], Ellyse R. Thomas[1], Graylin M. Skates[1], Natalie L. Johnson[1], Andy A. Chavez[1], Sophia R. Iaconis[1], Emma Janke[2], Yun-Feng Zhang[2,3], Minghong Ma[1], Daniel W. Wesson[2]

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Learning to correctly respond to odors guides foraging, danger avoidance, and social communication. However, the neural circuitry underlying emotional odor learning and behavioral responses to learned odors remains unknown. Our lab recently identified that two cell types encoding the dopamine D1 and D2 receptors (*drd1* and *drd2*) within the basolateral amygdala (BLA) form parallel glutamatergic pathways for communication with the ventral striatum. To determine how these ventral striatum projecting BLA circuits direct emotional behaviors, we optogenetically stimulated or chemogenetically inhibited the *drd1+* or *drd2+* BLA neurons that project to either the nucleus accumbens or the tubular striatum while mice engaged in a real time place preference/aversion task or an odor-shock Pavlovian fear learning paradigm. Using this strategy, we found that these parallel pathways distinctly influence both learned and unlearned negative emotional states when they are activated or suppressed, and do so depending upon their synaptic target in the ventral striatum – with unique contributions of *drd1+* nucleus accumbens projecting versus *drd2+* tubular striatum projecting BLA neurons. Ongoing work utilizing two-photon calcium imaging will investigate the striatum projecting amygdalar ensemble encoding of emotional odor learning. These results expand our understanding of how odors acquire emotional significance and reveal insights into how amygdala-striatal circuitry orchestrates emotional responses to odors.

Stability And Flexibility Of Neural Representations In The Olfactory Tubercle

Venkatesh N Murthy
Harvard University, Cambridge, MA, United States

Learning-induced changes in neural activity can occur rapidly and differentially in distinct types of neurons in the olfactory tubercle (OT; also referred to as the tubular striatum). Such remodeling of activity results in representations that reflect the valence of the odor cues. Recently, we reported that D1 receptor expressing neurons in the OT robustly and bidirectionally represented odor valence, responding similarly to odors predicting similar outcomes regardless of odor identity. Another major class of OT neurons, the D2 receptor expressing ones, showed weaker neuronal representation of odor-outcome associations and were more selective for odor identity than valence. These and other studies have clearly shown that the odor responses in the OT are highly plastic, allowing the valence representation to be rapidly updated in different circumstances. However, it is unclear whether and how neural representations in the OT change when animals learn new associations, or when the odor-outcome contingencies for older odors are degraded. We performed two-photon calcium imaging of D1 and D2 receptor expressing neuronal populations in the OT of mice trained in an odor-reward Pavlovian conditioning task. After mice have learnt specific odor-outcome associations, neuronal responses were surprisingly labile over several days even though mouse behavior was stable. We will present data from ongoing experiments aimed at testing how this representational stability varies with different schedule of odor experiences and learning. Together, our studies will shed light on how the OT neural population balances flexibility during learning with stability for longer-term memory of these learnt associations.

Potential Role Of Islands Of Calleja In Regulating Grooming And Depression-Like Behavior In Mice

Minghong Ma
Department of Neuroscience, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States

The ventral striatum is a reward center, comprising multiple subdivisions. The islands of Calleja (IC) contain clusters of densely packed granule cells, predominantly situated in the olfactory tubercle (OT). The IC are evolutionally conserved, charaterized by expression of the D3 dopmaine receptor. Optogenetic activation of OT D3 neurons robustly initiates self-grooming in mice while suppressing other ongoing behaviors. Conversely, optogenetic inhibition of these neurons halts ongoing grooming, and genetic ablation reduces spontaneous grooming. As abnormal self-grooming is often observed in mouse models of affective disorders, we invesgiated the potential role of OT D3 neurons in depression-like behavior. Chronic restraint stress (CRS) induces robust depression-like behaviors in mice and decreases excitability of OT D3 neurons. Ablation or inhibition of these neurons leads to depression-like behaviors, whereas their activation ameliorates CRS-induced depression-like behaviors. Moreover, activation of OT D3 neurons has a rewarding effect, which diminishes when grooming is blocked. Finally, we propose a model that explains how OT D3 neurons may influence dopamine release via synaptic connections with OT spiny projection neurons that project to midbrain dopamine neurons. These studies reveal a crucial role of OT D3 neurons in bidirectionally mediating self-grooming and depression-like behaviors, suggesting a potential therapeutic target.

11:50 **Q& A Panel**

12:30 - 2:00 PM	Calusa ABC
How can we do better? Disruptive ideas for understanding olfaction and taste in natural contexts	

As experimentalists attempting to understand the neural basis of smell and taste, we are forced to make choices about which stimuli to use, how we present them, how we measure perception, and the range of odor- or taste-guided behaviors we study. As a result, our collective understanding of the neural mechanisms underlying chemosensation derives from a body of work that can be driven by experimental practicalities and divorced from the realities of how animals experience and respond to olfactory and gustatory signals in their natural environment. Despite key discoveries and game-changing advances in technologies for probing neural mechanisms and behavior, placing experimental findings in a naturalistic context remains a challenge that, we argue, receives too little attention. Here, we bring together a panel of scientists with expertise in diverse areas of chemosensory neuroscience to share their perspectives on advancing our understanding of how smell and taste actually work in the natural world. The panel will feature ample time for discussion and debate, including input from the audience, on ways of approaching chemosensory neuroscience from a more naturalistic perspective – and how a failure to do so might lead us astray.

Moderators

Alfredo Fontanini, SUNY Stonybrook
Leslie Kay, University of Chicago

Chair(s): Matthew Wachowiak and Elizabeth Hong

1 **Panelist - Matt Wachowiak, University Of Utah School Of Medicine**

2 **Panelist - Elizabeth J. Hong, California Institute Of Technology**

3 **Panelist - Adam Dewan, Florida State University**

4 **Panelist - Don Katz, Brandeis University**

5 **Panelist - Lisa Stowers, Scripps Research Institute**

2:00 - 4:00 PM	Calusa EFGH
Neuromodulation of Chemosensation	

Chair(s): Natale Sciolino & John Boughter

Neuromodulation And Chemosensation: From Dynamics To Function

Natale Sciolino[1], John Boughter[2]

[1]University of Connecticut, Storrs, CT, United States, [2]University of Tennessee Health Sciences Center Memphis, Memphis, TN, United States

Neuromodulators are essential for shaping sensory information processing, and conversely salient sensory information regulates the dynamics of neuromodulatory systems. The activates and functions of neuromodulators have been historically difficult to study in vivo. Recent advancements in optical imaging, chemical sensors, and optogenetics have allowed scientists to better understand the interaction of neuromodulatory circuits and sensory systems. This symposium highlights cutting-edge tools that reveal how neuromodulators like acetylcholine, norepinephrine, dopamine, and neuropeptide Y influence taste and odor processing and how chemosensory information influences neuromodulatory signaling in both rodents and humans. These interactions between chemosensation and neuromodulation help organisms make appropriate feeding decisions and adjust their behavior based on physiological needs and external cues.

Neuromodulation In The Gustatory Cortex And Its Involvement In Taste Behaviors

Mia B. Fox[1], Walt J. Krueger[1], Stephanie M. Staszko[2], John D. Boughter Jr.[1], Max L. Fletcher[1]

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The neuromodulator acetylcholine (ACh) is released in various cortical areas in association with functions such as novelty, learning, and attention. Previous studies show its release in gustatory cortex (GC) plays an important role in both taste neophobia and conditioned taste aversion (CTA) behaviors. We used neuronal tracing and immunocytochemistry to delineate cholinergic input to the GC from the basal forebrain (BF) in mice. 73% of GC-projecting neurons in BF were cholinergic, positive for choline acetyltransferase (ChAT). Immunocytochemistry revealed the presence of (muscarinic) M1 and M2 receptors in GC. Behavioral experiments with either systemically administered or direct cortical infusion of scopolamine (ACh antagonist) indicate that blocking muscarinic receptors does not affect the neophobic response to a novel stimulus, but it interferes with either attenuation of neophobia or expression of a conditioned taste aversion (CTA). We are currently conducting calcium imaging studies investigating the activity of cholinergic neurons during taste neophobia. GCaMP was expressed in, and microendoscopes implanted into, the BF of Chat-cre mice. Finally, simultaneous electrophysiological recordings of BF and GC demonstrate increased theta coherence between these structures that becomes more aligned to consumption with familiarity.

Locus Coeruleus Noradrenergic Modulation Of Cortical Taste Processing

Will Fan, Natale R. Sciolino
University of Connecticut, Storrs, CT, United States

Neuromodulatory systems adaptively regulate the computations performed by neural circuits, yet their involvement in central taste processing is largely unexplored. The primary gustatory cortex (GC) receives a prominent neuromodulatory input from noradrenergic neurons in the locus coeruleus (LC), which plays a well-established role in shaping sensory perception. LC neurons exhibit phasic firing in response to salient events and elevated tonic activity in stressed or high-arousal states. To investigate how phasic and tonic LC activity influences GC taste processing, we used miniscope calcium imaging to record taste-evoked responses of GC neurons while optogenetically activating LC axons using different stimulation patterns. We found that activation of LC axons produced heterogeneous changes in the response dynamics of a subset of GC neurons, reshaping their taste response profiles. Assessment of response sparseness, taste quality encoding, and palatability encoding revealed that LC's modulatory effects depend on its activity pattern. Specifically, phasic LC output tended to enhance taste encoding, whereas elevated tonic LC output impaired it. These findings highlight the intricacy of neuromodulation in sensory systems and the flexibility of cortical taste processing, offering new insights into how behavioral states shape food perception.

2:51 **Beyond Reward Prediction Errors: A Temporal Difference Model Of Dopamine That Can Account For Sensory Prediction Errors**

Matthew Gardner
Department of Psychology, Concordia University, Montreal, QC, Canada

Dopamine Differentially Encodes Sucrose Across The Acquisition And Extinction Of A Conditioned Taste Aversion

Maxine K. Loh[1,2], Samantha J. Hurh[2], Paula Bazzino[3], Rachel M. Donka[2], Alexandra T. Keinath[2], Jamie D. Roitman[2], Mitchell F. Roitman[2,3]

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United States, [3]Graduate Program in Neuroscience, University of Illinois at Chicago, Chicago, IL, United States

Mesolimbic dopamine encoding of non-contingent rewards and reward-predictive cues has been well established. Considerable debate remains over how mesolimbic dopamine responds to aversion in contrast to reward. Inconsistencies may arise from the use of aversive stimuli transduced along different neural paths relative to reward or the conflation of responses to avoidance and aversion. In rats, we measured behavioral and dopamine responses in vivo to the changing valence of intraoral sucrose via DeepLabCut and fiber photometry. Pairing sucrose tasting with malaise via injection of lithium chloride (LiCl) drove the development of a conditioned taste aversion (CTA) and rendered the typically rewarding taste of sucrose aversive upon subsequent re-exposure. Following CTA formation, intraoral sucrose suppressed phasic ventral tegmental area dopamine (VTA_{DA}) neuronal activity and nucleus accumbens dopamine release while increasing behavioral reactivity (nose and forepaw movement). This pattern of dopamine signaling and behavioral reactivity after CTA is similar to intraoral infusions of innately aversive quinine and contrasts with that to sucrose when it was novel or not paired with LiCl. Dopamine responses were negatively correlated with behavioral reactivity to intraoral sucrose and predicted home cage sucrose preference. Further, the strength of the CTA modulated phasic dopamine responses to sucrose, which were further suppressed by repeated LiCl pairings and recovered through extinction. Together, these findings demonstrate differential dopamine encoding of the same taste stimulus according to its valence, which is aligned to distinct behavioral responses.

A Thirst-Dependent Odor Spotlight

Silvia Huerta Lopez, Katie McShea, Stephen Liberles
Howard Hughes Medical Institute, Department of Cell Biology, Harvard Medical School, Boston, MA, USA, Boston, MA, United States

Internal states, such as hunger and thirst, are powerful motivational states that shape sensory perception, enhancing attention to need-relevant cues. Here, we investigate how thirst differentially influences odor perception, selectively heightening attraction to drink odors while sparing responses to other attractive cues, such as pheromones. The mouse olfactory system detects diverse odors that drive behaviorally specific responses, yet how distinct physiological states modulate sensory pathways to drive state-appropriate behaviors remains unclear. Our studies aim to uncover the molecular and circuit mechanisms by which thirst selectively modulates odor responses, providing insight into how internal states dynamically influence sensory processing and behavior.

2:00 - 4:10 PM	Calusa ABC
Eating with Feeling: Exploring Connections Between Emotions and Chemosensory Stimuli	

Chair(s): Kathryn Deibler, Xiaorong (Phoebe) Su, Casey Trimmer, Dan Wesson, Theresa White

2:00 **Eating With Feeling: Exploring Connections Between Emotions And Chemosensory Stimuli**

Kathryn Deibler[1], Xiaorong (Phoebe) Su[2], Casey Trimmer[3], Dan Wesson[4], Theresa White[5]
[1]Flavour Essentials, [3]Firmenich, [4]University of Florida, [5]Le Moyne College

Understanding the interplay between emotions and chemosensory stimuli presents significant opportunities for industries focused on product development in food, fragrance, and other consumer goods. This presentation will explore the neurobiological and psychological foundations that link emotional processing with the chemical senses, specifically olfaction and gustation. Furthermore, advancements in the measurement of emotional responses to chemosensory stimuli, such as augmented reality, large language models, generative AI, and neuroimaging, will be examined in conjunction with traditional models such as psychophysics and electroencephalography (EEG), highlighting potential multi-component approaches to innovative product applications. This discussion will focus on practical insights for industry professionals, emphasizing how a deeper understanding of emotional arousal and chemical senses can inform the design of products that evoke desired emotional responses, enhancing consumer satisfaction. By bridging the gap between sensory science and emotional response, this research has the potential to revolutionize approaches to flavor, fragrance, and product development across various sectors.

2:05 **Exploring The Interplay Between Emotions And Chemosensory Stimuli**

Rachel Herz
Department of Psychiatry and Human Behavior, Brown University Medical School

I will review basic methods for examining how emotions can influence chemosensory perception and how chemosensory stimuli can influence emotional states and provide illustrative examples from taste and olfactory research. I will then discuss new work using olfactory virtual reality that demonstrates heightened emotional outcomes. I will conclude by reviewing the importance of considering individual differences and external factors when evaluating emotional responses in chemosensory research.

2:28 **A Multicomponential Approach To Emotional Experiences: The Case Of Relaxing And Stimulating Odors**

Géraldine Coppin
UniDistance Suisse & Swiss Center for Affective Sciences, University of Geneva

According to the multicomponential approach to emotional experiences, an emotion is a multi-component response triggered by the way an event is appraised by an individual. This first emotional component – appraisal – depends on the individual's current concerns, values, and goals. This component triggers an emotional response involving four other components: autonomic physiology, action tendency, expression, and feeling. The feeling component (or emotional experience) is often defined by a combination of valence (i.e., felt pleasure/displeasure) and arousal (i.e., felt calm/energy). Here we will discuss data testing whether the so-called "arousal effects" of odors can be identified via subjective reports, implicit measures, brain imaging data and peripheral physiology, while controlling for valence. We will first consider the subjective experience of relaxation or stimulation through cross-cultural experiments conducted in different languages. We will then show that the verbal report of a feeling is accompanied by implicit processing that reveals privileged associations between certain odors and their relaxing or stimulating properties. We will also discuss results on the short-term cerebral consequences of exposure to relaxing and stimulating odors. Finally, we will investigate the short-term physiological consequences of exposure to either relaxing or stimulating odors. This research will highlight the advantage of a multi-component approach to emotional experiences for fundamental research but also for applied and industrial research.

2:50 **From Flavor To Feeling: Symrise'S Neuroscientific Exploration Of Emotional Connections In Taste**

Mansi Patney, Jonathan Jacobs
Symrise AG

Emotional connections to flavors play a key role in shaping consumer preferences, as specific tastes and aromas can evoke powerful memories and emotions, enhancing product appeal and satisfaction. Flavors that hold cultural significance and tied to positive memories are more likely to be preferred, as they activate pleasure centers in the brain and foster brand loyalty (Herz, 2010; Prescott, 2012). Neuroscience offers valuable insights into consumer behavior by measuring subconscious responses that traditional methods may miss. Techniques like electroencephalography (EEG) provide a more nuanced understanding of decision-making (Plassmann et al., 2015; Ariely & Berns, 2010). EEG measures electrical potential differences on the scalp, allowing researchers to assess neural responses to stimuli in real-time, revealing implicit emotional and cognitive associations without relying on verbal feedback. This study assesses consumer perceptions of two flavors for pain medication. Using the Symrise gen-isys neuroscience program, we employed EEG with 30 blindfolded male and female participants, ages 18-55, who are regular users of over-the-counter pain medication. Self-evaluation scores showed parity, while EEG results provided deeper insights into the emotional appeal and preference for the two flavors, demonstrating EEG's ability to capture reliable, objective insights into emotional connections that self-reported data might overlook. These insights offer valuable guidance for product development and flavor optimization, highlighting the importance of balancing liking and excitement to drive consumer preference.

3:08 **Generative Ai In Sensory Science: Data Crunching To Consumer Understanding**

Michelle Murphy Niedziela
Nerdoscientist LLC

The integration of generative AI technologies into sensory research holds promise for advancing our understanding of consumer responses to taste and smell. Generative AI tools, such as large language models, have demonstrated potential in automating the analysis of qualitative data, expediting thematic coding, and identifying patterns within consumer narratives. Moving beyond these established applications, this talk will explore the capacity of generative AI to enhance experimental design, simulate real-world sensory environments, and facilitate cross-modal insights. Using AI-driven virtual and augmented reality environments enables the recreation of ecologically valid contexts-such as noisy restaurants or serene outdoor settings-that are crucial for assessing sensory experiences in realistic conditions. AI's ability to model complex environmental variables, including ambient noise, lighting, and temperature, contributes to a more comprehensive understanding of how context influences sensory perception and satisfaction. Adaptive AI environments and chatbots can dynamically adjust to participant responses, offering novel approaches for studying the fluid and context-dependent nature of sensory experiences. The integration of behavioral science frameworks, such as decision-making models and theories of multisensory integration, enhances the interpretive value of AI-generated data, ensuring that insights, remain consumer-centric and actionable. Ethical considerations and the challenges of balancing technological advancements with consumer-focused research will also be discussed. The potential of generative AI to transform sensory research offers new methodologies that align with behavioral science principles and provides opportunities for more efficient, robust, and ecologically valid studies.

3:30 **Arousal And The Modulation Of Food-Related Perceptions And Emotions**

John Prescott
Università degli Studi di Firenze, Italy & TasteMatters Research & Consulting, Australia

Across sensory systems, several stimulus collative characteristics, including intensity, novelty, complexity, and perceived threat, are known to elicit high levels of physiological and psychological arousal. Arousal and arousability are important elements in the emotional response to stimuli generally, but also specifically to foods, ultimately influencing food preferences and choices. In particular, food rejections are frequently linked to such arousal-inducing characteristics. Responses to food sensory properties are subject not just to variations in perceptual sensitivity due to genetics or experience – as in the case of widely rejected qualities such as bitterness or pungency - but also to the arousal potential of those stimuli. Moreover, this is linked to various enduring aspects of personality, suggesting that the impact of arousal on food choices is merely one aspect of a more general sensory sensitivity. The impact of diet on various health outcomes underlines the importance of understanding the relationship of arousal to food-related emotions and food choices.

3:52 **How Reckitt Leverages Emotions To Better Understand The Consumer**

Stephen Lillford[1], Neeta Yousaf[2]
[1]Reckitt, [2]Curion Insights

There is no shortage of techniques available to measure emotional reactions. Explicit measures like Snoopy Scales and emotion word lists such as EsSense25 and PANAS have provided for decades the ability to measure rational (System 2) emotional associations, whereas implicit (System 1) approaches such as IRT provide a measurement of the strength of more complex conceptual associations. Biometrics are yet another way to measure something about the human emotional experience. With all of these options, the challenge we have is not finding the perfect technique, but developing a research program to bridge the science with organizational needs and downstream decisions to benefit the consumer experience.

In this presentation Stephen and Michael will explain how Reckitt Benckiser has navigated these challenges to develop a robust program to measure emotions and help create products that truly go “beyond liking” by prioritizing emotional KPIs. Real life data will be shown comparing the performance of implicit and explicit measures providing clues to the underlying choice and decision processes consumers use to internalize product experiences and make choices. Finally we’ll discuss a bit about the difficult change needed to create a product where Liking is not the major KPI.

4:00 - 4:30 PM	Estero Foyer
Coffee Break	

4:15 - 6:00 PM	Estero Ballroom
Don Tucker Memorial and Undergraduate Research Awards Poster Session	

400 **Don Tucker Finalist: Estrogen Alters Fatty Acid Signaling In Type Ii Taste Cells**

Emeline Masterson[1,2], Kaylee Perez[1,2], Naima Dahir[1,2], Timothy Gilbertson[2]

[1]Burnett School of Biomedical Sciences, College of Medicine, University of Central Florida, Orlando, FL, United States, [2]Department of Internal Medicine, College of Medicine, University of Central Florida, Orlando, FL, United States

Our recent work has highlighted the influence of several hormones on fat taste, dietary fat preference, and subsequent fat intake, including adiponectin, ghrelin, and estrogen. Of these, estrogen seems to exert the most significant influence over the taste of fat. Expression data shows that the G protein-coupled estrogen receptor (GPER1) and ERα are highly expressed in taste cells. The former directly influences fatty acid signaling in real-time by enhancing responsiveness to fatty acids in patch clamp and calcium imaging studies. To examine this in greater detail we are using a multidisciplinary approach to identify the cellular targets of estrogen's action within specific cell types. Using genetically identifiable taste cells, we have found that Type II cells are the primary target of estrogen in both males and females. Estrogen treatment increased linoleic acid-induced currents and modulated intracellular calcium in isolated taste cells from GFP-PLCß+ mice. Moreover, the ability of estrogen to dynamically affect fatty acid responsiveness in taste cells was estrus cycle dependent. In females with high circulating estrogen, there is little enhancement, while in those with low levels of circulating estrogen, and in males, estrogen significantly increased cellular and behavioral fatty acid responses. Utilizing immunohistochemistry, pharmacology, electrophysiology, and imaging techniques we found that Trpm4 and Trpm5 channel expression and function exhibit sex-dependent differences, influenced by distinct estrogenic regulatory mechanisms. We hypothesize that these differences may contribute to the differences in fatty acid taste seen in male and female mice. Our findings underscore the complex interplay between sex hormones, TRP channels, and taste cell activation in shaping fat taste perception.

401 **Don Tucker Finalist: Locus Coeruleus Noradrenergic Modulation Of Cortical Taste Processing**

Will Fan, Natale R. Sciolino
University of Connecticut, Storrs, CT, United States

Neuromodulatory systems adaptively regulate the computations performed by neural circuits, yet their involvement in central taste processing is largely unexplored. The primary gustatory cortex (GC) receives a prominent neuromodulatory input from noradrenergic neurons in the locus coeruleus (LC), which plays a well-established role in shaping sensory perception. LC neurons exhibit phasic firing in response to salient events and elevated tonic activity in stressed or high-arousal states. To investigate how phasic and tonic LC activity influences GC taste processing, we used miniscope calcium imaging to record taste-evoked responses of GC neurons while optogenetically activating LC axons using different stimulation patterns. We found that activation of LC axons produced heterogeneous changes in the response dynamics of a subset of GC neurons, reshaping their taste response profiles. Assessment of response sparseness, taste quality encoding, and palatability encoding revealed that LC's modulatory effects depend on its activity pattern. Specifically, phasic LC output tended to enhance taste encoding, whereas elevated tonic LC output impaired it. These findings highlight the intricacy of neuromodulation in sensory systems and the flexibility of cortical taste processing, offering new insights into how behavioral states shape food perception.

402 **Achems Undergrad Finalist: Oleate And Linoleate Fatty Acid Oral Detection Thresholds In Humans**

Samuel I Deutsch[1], Nicholas Amado[1], Paul A.S. Breslin[1,2]

[1]Rutgers University, New Brunswick, NJ, United States, [2]Monell Chemical Senses Center, Philadelphia, PA, United States

Fatty acid detection thresholds in humans have been reported to range from 1-10 mM. Various methodologies have been used in these studies that yield variable and high thresholds. Our aim was to determine thresholds for oleic and linoleic acid sodium salts in humans with a highly sensitive measure. The deprotonated form of fatty acids has been shown in vitro to preferentially interact with oral fatty acid receptors, such as CD36. 10 humans were given a two-alternative forced-choice (2-AFC) threshold test containing the sodium salts of oleic acid (NaOleate) and linoleic acid (NaLinoleate) dissolved in water using a modified staircase procedure with a four-down, one-up rule. The sodium salts of the fatty acids were chosen due to their relatively high solubility in water. The 2-AFC tests were run twice for each participant and the thresholds were averaged to determine an absolute threshold. Participants wore nose clips to remove olfactory cues. The absolute oral detection thresholds ranged from 0.28mM to 1.18mM across the tested subjects. These results suggest that humans can reliably detect fatty acid sodium salts within the concentration range of 200 to 1000 micromolar, approximating in vitro receptor sensitivities. Our future work will look at testing other fatty acids using the sodium salt and the same methodology to understand if there are differences in sensitivities based on the adiposity of subjects.

403 **Don Tucker Finalist: Metabolic Modulation Of Appetitive Odor Processing In Food Reward Valuation**

Androula Savva[1,2], Marc Guitart-Masip[3,4,5], Ata Ghaderi[1], Cynthia M. Bulik[2,6,7], Janina Seubert[1]

[1]Department of Clinical Neuroscience, Psychology Division, Karolinska Institutet, Stockholm, Sweden, [2]Department of Medical Epidemiology and Biostatistics, Centre for Eating Disorders Innovation, Karolinska Institutet, Stockholm, Sweden, [3]Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden, [4]Center for Psychiatry Research, Region Stockholm, Stockholm, Sweden, [5]Center for Cognitive and Computational Neuropsychiatry (CCNP), Karolinska Institutet, Stockholm, Sweden, [6]Department of Psychiatry, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States, [7]Department of Nutrition, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States

Hunger is a powerful motivational state that enhances both the hedonic value of food and the drive to pursue food rewards. In this state, sensory cues, particularly odors, play a key role in triggering anticipatory reward responses, motivating individuals to seek and consume food. Unlike visual or auditory cues, odors are uniquely effective in evoking memories of food and eliciting physiological responses that prepare the body for food intake. However, the specific mechanisms by which food odors invigorate reward-driven actions, and how these effects vary by metabolic state, remain poorly understood. In this study, we present a novel experimental paradigm that separates invigorating effects of food stimuli on reward-seeking behavior, across two sensory modalities. In a food incentive delay paradigm, participants completed a reaction time task in which they could earn points that were exchanged for snacks at the end of the study. Participants (N=48) attended two experimental sessions after an overnight fast and completed the study once while hungry and once after consuming a standardized ad libitum breakfast. Prior to each trial (rewarded, non-rewarded), participants were presented with either an odor or a picture (food, non-food) and were instructed to press a button as soon as a symbol appeared on the screen. Our results indicate that hunger selectively improves reward-seeking performance when the task is preceded by a food odor, but not a food picture. Additionally, food and non-food stimuli elicit no differentiable invigorating effects on reward-seeking behavior in a satiated state. Taken together, these findings highlight the distinct role of odors in driving reward-seeking behavior in hunger and open up unique avenues of investigation into populations with maladaptive eating behaviors.

404 **Don Tucker Finalist: Basolateral Amygdala Circuitry Linked To The Ventral Striatum Underlies Emotional Responses To Odors**

Sarah E. Sniffen[1], Sang Eun Ryu[1], Milayna M. Kokoska[1], Janardhan Bhattarai[2], Yingqi Wang[2], Ellyse R. Thomas[1], Graylin M. Skates[1], Natalie L. Johnson[1], Andy A. Chavez[1], Sophia R. Iaconis[1], Emma Janke[2], Yun-Feng Zhang[2,3], Minghong Ma[2], Daniel W. Wesson[1]

[1]Depts of Neuroscience and Pharmacology & Therapeutics, Florida Chemical Senses Institute, University of Florida, Gainesville, FL, United States, [2]Dept of Neuroscience, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States, [3]State Key Laboratory of Integrated Management of Pest Insects and Rodents, Institute of Zoology, Chinese Academy of Sciences, Beijing, China

The basolateral amygdala (BLA) acts as a critical hub for regulating emotional responses to odors, yet the cell types and circuitry by which the amygdala orchestrates these responses remain poorly understood. Here, using a combination of viral tracing, optogenetic stimulation, and chemogenetic inhibition, we identified two cell types encoding the dopamine D1 and D2 receptors (*drd1* and *drd2*) within the BLA that form parallel pathways for communication with the ventral striatum. These neurons arise from the basal nucleus of the BLA, innervate the entire space of the ventral striatum (both the nucleus accumbens and the tubular striatum), and are capable of exciting ventral striatum neurons. Interestingly, these BLA neurons primarily form ipsilateral pathways with one ventral striatum target region but can also collateralize to both ventral striatum subregions. Further, we found that the *drd1*+ and *drd2*+ parallel pathways distinctly influence both learned and unlearned negative emotional states when they are activated or suppressed, and do so depending upon where they synapse in the ventral striatum – with unique contributions of *drd1*+ and *drd2*+ nucleus accumbens projecting versus tubular striatum projecting BLA neurons. Overall, these results contribute to a model whereby parallel, genetically-distinct BLA to ventral striatum circuits inform emotional states in a projection-specific manner, and expand our understanding of how odors acquire emotional significance. Ongoing work utilizing two-photon calcium imaging will investigate how striatum projecting amygdala ensembles adapt their coding strategies throughout learning to guide emotional responses, further elucidating how emotions influence processing of chemosensory stimuli.

405 **Don Tucker Finalist: Palatability And Post-Prandial Glycemic Responses Of Breads Enriched With Soybean Flour**

Stephanie Okoye[1], Rachel Carlson[2], David Dohem[2], Kenneth Dallmier[3], Yanina M. Pepino[1,4,5]

[1]Division of Nutritional Sciences, University of Illinois Urbana-Champaign, Urbana, IL, United States, [2]Northern Crops Institute, Fargo, ND, United States, [3]Demand Side Ag, Mahomet, IL, United States, [4]Food Science and Human Nutrition, University of Illinois Urbana-Champaign, Urbana, IL, United States, [5]Carle Illinois College of Medicine, Urbana, IL, United States

Bread, a carbohydrate-rich staple food, is a primary calorie source in many regions worldwide but often lacks balanced nutritional value. This study aimed to address two key objectives: first, to determine whether replacing

a portion of wheat flour with soy flour in bread, thereby increasing dietary protein, reduced postprandial blood glucose excursions without increasing insulin spikes in individuals with overweight or obesity. Second, to evaluate whether the modified bread maintains sensory appeal for consumers. Using a within-subject design, 10 adults (5 males, 5 females) without diabetes (age 32 years (SD 5); BMI 30.53 kg/m^2 (SD 3.16)) participated in three study visits. In a quasi-randomized order, they consumed isocaloric portions of bread containing 0% (control), 10%, or 30% soy flour. Blood samples were collected via intravenous catheter before and at multiple intervals within two hours after bread consumption to measure plasma glucose and insulin concentrations. Participants also rated hunger, satiety, and product liking using visual analog scales. Results showed a dose-response relationship between soy flour content and reductions in plasma glucose over time, peak plasma glucose, and glucose area under the curve (AUC) (all p values <0.05) with no differences in insulin concentrations between bread conditions. The 30% soy flour bread significantly reduced peak glucose and AUC compared to the control bread ($p < 0.05$), while the values for the 10% soy flour bread were intermediate between the 0% and 30% soy flour. All breads were equally liked, and there were no differences in hunger or satiety ratings (all $p > 0.1$). These findings suggest enriching bread with at least 30% soy flour may optimize metabolic benefits by reducing postprandial glucose spikes without compromising sensory appeal.

406 **Don Tucker Finalist: Genetically-Heterogeneous Orexin-A Inputs To The Mouse Olfactory Bulb Modulate Mitral/Tufted Cells Via Orexin Receptor Type 1 And 2**

Meizhu Qi[1,2], Debra Fadool[1,2,3], Douglas Storace[1,2,3]
[1]Department of Biological Science, Tallahassee, FL, United States, [2]Program in Neuroscience, Tallahassee, FL, United States, [3]Institute of Molecular Biophysics, Tallahassee, FL, United States

The olfactory bulb (OB) receives direct projections from the lateral hypothalamus that includes a population of neurons expressing the neuropeptide orexin-A. These neurons are genetically heterogeneous, with distinct subsets that co-express vesicular glutamate transporters (VGLUT1 or VGLUT2). Herein, we used a combination of virally-mediated anterograde tract tracing and immunohistochemistry to map orexin-A inputs in the OB with high-resolution confocal microscopy and used slice electrophysiology to better understand the functional role of orexin-A inputs. Orexin-A expression was broadly distributed throughout the OB, with similar expression density in different anatomical layers and across the anterior-posterior axis. Morphological analysis of orexin-A axon terminals revealed that 67% co-expressed VGLUT2. The remainder either co-expressed VGLUT1 or lacked glutamatergic markers. A total of 111 mitral/tufted cells (M/TCs) were current-clamped in the whole-cell configuration, whereby evoked currents were elicited in the presence of synaptic blockers. Bath application of 100 nM orexin-A modulated action potential (AP) firing frequency in 79% of M/TCs, with 49% inhibited (decrease AP firing frequency 0.51) and 51% excited (increase AP firing frequency 0.85). The orexin-R type I antagonist (SB-334867-A) changed the AP firing frequency compared with orexin-A alone in 9 of 15 cells, whereas the orexin-R type 2 antagonist (TCS-OX2-29) affected AP firing frequency in 7 of 10 cells. This suggests that both type I and 2 receptors contribute to orexin A modulation of M/TCs. The results highlight the genetic heterogeneity of orexin-A inputs to the OB and provide new insights into the complex mechanisms underlying orexin-A modulation of olfactory sensory processing.

407 **Don Tucker Finalist: Odor Encoding In The Dorsal Tenia Tecta, An Under-Explored Area Of Primary Olfactory Cortex**

Sam A Caton, Austin Pauley, Cecilia Bouaichi, Roberto Vincis, Adam Dewan
Florida State University, Tallahassee, FL, United States

To understand the mechanisms underlying olfactory perception, it is important to determine the function and processing that occurs in each individual component of the network. While putative functions have been ascribed to many areas of primary olfactory cortex, the contribution of the dorsal tenia tecta (DTT) to olfactory processing remains severely understudied. Despite the DTT's classification as part of the primary olfactory cortex, prior studies have hinted that that this region is anatomically and functionally distinct from other olfactory cortical areas. Specifically, the cytoarchitecture of the DTT shares more similarities with the hippocampus than other primary olfactory cortical regions and it only receives sparse input from the olfactory bulb. This project explores the odor encoding properties of DTT neurons using a combination of high-density electrophysiological recordings and microendoscope calcium imaging with precise odor delivery. We find that despite sparse input from the olfactory bulb, DTT neurons are sensitive to sniffing behavior and can encode both odor identity and concentration. We have further dissected these initial findings by focusing on the odor coding properties of genetically defined neural subpopulations. We find that both GABAergic and glutamatergic neurons dynamically respond to odor in a predominantly excitatory manner and that either subpopulation alone is sufficient to determine odor identity or concentration above chance levels using decoding analysis. This research furthers our understanding of the odor response properties of the DTT and provides a foundation to explore its contribution to olfactory perception.

408 **Achems Undergrad Finalist: Unifying Odor And Place In The Mouse Olfactory Bulb**

Sidney E. Rafilson, Nate Gonzales-Hess, Casey Lennon-Jones, Aldis P. Weible, Matthew C. Smear
University of Oregon, Eugene, OR, United States

Mammals sniff to sample odors, enabling them to actively sense the chemical world. These samples help identify odorous objects, as well as locations and events. However, there is no receptor for place or time. To interpret olfactory information, the brain must contextualize odor-driven activity with signals about when, where, and how they sniffed. Recent work from our lab has shown that mice structure their breathing into persistent rhythmic states that synchronize with state-like patterns in the spiking activity and local field potentials (LFPs) of the olfactory bulb (OB). Additionally, we identified "place cells" in the OB and demonstrated that an animal's

location can be decoded from OB population dynamics. These findings suggest that sensory information is integrated with internal models of place and time as soon as it enters the brain. To investigate the formation of these early contextual signals in the OB, we used methimazole (MMZ) as a chemical scalpel to induce anosmia. By ablating olfactory sensory neurons with MMZ, we characterized the dynamics of OB place coding in the absence of sensory inputs. Furthermore, we show that MMZ treatment disrupts rhythmic sniffing, the associated neural states, and OB-hippocampus (HC) LFP coupling. These findings suggest that sniffing functions as an internal clock, synchronizing sensory and contextual information across brain regions. More broadly, this work highlights how the brain integrates sensory inputs with internal dynamics to construct a cohesive representation of the world.

409 **Achems Undergrad Finalist: Revealing Explicit Odor Intensity Ratings With Relative Readouts**

Aiden Streleckis[1], Robert Pellegrino[1], Beatrice Barra[2], Matthew Andres[1], Jacqueline Zhao[2], Dmitry Rinberg[2], Joel D. Mainland[1,3]

[1]Monell Chemical Senses Center, Philadelphia, PA, United States, [2]Neuroscience Institute, New York University Langone Health, New York, NY, United States, [3]Department of Neuroscience, University of Pennsylvania, Philadelphia, PA, United States

Odor intensity is essential to odor perception, enabling an organism to decipher the proximity or location of an odor stimulus. Understanding the neural mechanisms behind the perception of odor intensity is critical to determining how the brain translates odor stimuli into perceivable sensations. Due to the chemical differences between different odorants, there is a disconnect between concentration and intensity: while one odor may be very intense at a given concentration, another may be undetectable at that same concentration. While understanding the relationship of concentration and intensity is easily assessed in humans using explicit ratings of intensity, we cannot obtain explicit ratings from model organisms. Due to this limitation, deciphering the neural mechanisms of odor intensity perception by deriving both perceptual and neural data from the same model organism presents difficulties. To measure perceived intensity in mice, we used a two-odor concentration discrimination task (2OCD) where intensity disparities across odors lead to systematic errors in the task. This allowed us to predict the concentrations at which two odors have equal perceived intensity. To validate this prediction, we replicated the mouse paradigm in humans and confirmed that the systematic errors correspond with explicit matched odor intensities. Our results confirm that explicit odor intensities are accurately predicted using the 2OCD paradigm, validating it as a measure of perceived intensity in mice. This methodology provides a powerful tool to investigate the neural encoding of perceived intensity in a mouse model.

410 **Don Tucker Finalist: The Role Of Tex15 In Shaping Stochastic Olfactory Receptor Gene Choice In Mouse Olfactory Epithelium**

Nusrath Yusuf[1], Jerome Kahiapo[1], David Brann[3], Alina Irvine[2], Josh Danoff[1], Alina Irvine[1], Pavithra Veera[1], Nader Boutros-Ghali[1], Bob Datta[3], Kevin Monahan[1]

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Each olfactory sensory neuron (OSN) expresses a single olfactory receptor (OR) allele, which encode the proteins that bind chemical odorants. In contrast, OSN progenitors co-express multiple OR genes during differentiation. The regulatory mechanisms that govern the transition to monogenic, monoallelic choice of an OR in a mature OSN needs to be elucidated. We show that testis expressed 15 (Tex15), a protein that has only been studied in the testes where it regulates methylation and silencing of transposons, is transiently expressed during this critical gene regulation window in OSN progenitors. By examining Tex15 KO mice, we show that Tex15 is crucial for stochastic OR gene choice. We find that when Tex15 is knocked out there is a dramatic reduction in the diversity of expressed OR genes with a few Class II OR genes dominating stochastic choice. These class II OR genes are the first to be transcriptionally activated in wild-type OSN progenitors. OSNs will still mature in the absence of Tex15 and continue to only express one chosen OR allele, however, the diversity of ORs expressed are vastly downregulated. Based upon its role in transposable element regulation, we hypothesized that Tex15 is regulating monoallelic OR gene choice through either methylation patterns or through its effect on chromatin state of developing OSNs. We also observe changes in methylation along several CpG sites and decrease in heterochromatin deposition over OR clusters and OR genes. This project elucidates a novel aspect of how OSNs come to stochastically choose a single OR and how Tex15 gene and protein guides this specific yet diverse choice.

7:00 - 9:00 PM	Calusa EFGH
Presidential Symposium: Motorizing the Chemical Senses	

Chair(s): Alfredo Fontanini

Motorizing The Chemical Senses
Alfredo Fontanini
Department of Neurobiology and Behavior, Stony Brook University, Stony Brook, NY, United States

Sensory processing and motor control are intimately linked. Animals use sensory information to guide and adjust movements and conversely move their sensors to actively sample the environment. In addition, perception and action are linked in the context of decision making. This is particularly the case for chemical senses, where the odor and the taste of a food are instrumental in guiding feeding behaviors. Despite this widely acknowledged relationship, sensory processing and motor control are still largely studied in isolation, as if they were independent processes. The goal of this symposium is to provide an integrative perspective on studying sensation and movement. The research presented relies on innovative behavioral approaches to analyze movements that are crucial to chemosensation. This symposium features work from four outstanding scientists. Jesse Goldberg will show how mice use their tongue to drink from a water spout that unexpectedly changes position and will present data on the role of the superior colliculus in touch-guided tongue control. Nicholas Hatsopoulos will discuss how monkeys use their tongue in the context of feeding and how motor and somatosensory cortices encode complex lingual shapes across a range of feeding behaviors. Dan Wesson will present research on how mice sniff to acquire odors and on the role of the mesolimbic dopaminergic system in promoting a switch from breathing to sniffing. Mitra Hartmann will present research on how rodents use their whiskers to determine the direction of air flow and on the importance of vibrissal vibrations in flow-sensing, a process with fundamental implications for odor plume detection. Altogether this symposium will highlight the importance of embracing a truly sensorimotor perspective in studying both chemosensation and movement.

A Collicular Map For Touch-Guided Tongue Control
Jesse Goldberg, Brendan Ito, Yongjie Gao, Brian Kardon
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Accurate goal-directed behavior requires the sense of touch to be integrated with information about body position and ongoing motion. Behaviors like chewing, swallowing, and speech critically depend on precise tactile events on a rapidly moving tongue, but neural circuits for dynamic touch-guided tongue control are unknown. Using high-speed videography, we examined 3D lingual kinematics as mice drank from a water spout that unexpectedly changed position during licking, requiring re-aiming in response to subtle contact events on the left, center, or right surface of the tongue. Mice integrated information about both precise touch events and tongue position to re-aim ensuing licks. Surprisingly, touch-guided re-aiming was unaffected by photoinactivation of tongue sensory, premotor, and motor cortices but was impaired by photoinactivation of the lateral superior colliculus (latSC). Electrophysiological recordings identified latSC neurons with mechanosensory receptive fields for precise touch events that were anchored in tongue-centered, head-centered, or conjunctive reference frames. Notably, latSC neurons also encoded tongue position before contact, information important for tongue-to-head based coordinate transformations underlying accurate touch-guided aiming. Viral tracing revealed tongue sensory inputs to the latSC from the lingual trigeminal nucleus, and optical microstimulation in the latSC revealed a topographic map for aiming licks. These findings demonstrate for the first time that touch-guided tongue control relies on a collicular mechanosensorimotor map, analogous to collicular visuomotor maps associated with visually-guided orienting across many species.

Cortical Encoding Of Primate Tongue Shape During Feeding
Nicholas Hatsopoulos, Callum Ross
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Dexterous tongue posture and movements underlies feeding behavior. The orofacial sensorimotor cortex has been implicated in the control of coordinated tongue kinematics, but little is known about how the brain encodes the tongue's 3D soft-body deformation. Here we combined 3D x-ray video radiography to track implanted markers on the tongue, multi-electrode cortical recordings, and machine learning-based decoding to explore the cortical representation of lingual kinematics in Rhesus macaque monkeys. From the marker positions on the tongue, we calculated a set of standard tongue kinematic metrics such as sagittal flexion, roll, protrusion, as well as regional lengths and widths. We also used a Procrustes superimposition to remove translational, rotational, and scale changes in tongue posture so as to isolate variables associated with tongue shape. We then trained a recurrent neural network to decode these kinematic and shape variables from orofacial primary motor (M1of) and somatosensory cortical (S1of) activity during feeding. We show that both standard kinematic metrics and complex lingual shapes across a range of feeding behaviors could be decoded with high accuracy consistent with previous studies of the arm and hand. However, decoding from M1of neural populations consistently outperformed similarly sized populations from S1of. We are currently examining whether neurons preferentially encode position/postural variables as compared to velocity variables.

Invigorating The Transition From A Breath To A Sniff
Dan Wesson
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The sniff is an essential component of both acquiring an odor and shaping the processing of odor information within the brain. Despite this importance, the neural systems which afford animals the ability to transition from basal breathing which serves the purpose of gas exchange, to engage in the voluntary act of sniffing, is unclear. We found that, in mice, dopamine release into two out of three ventral striatum subregions is coupled with bouts of sniffing and that stimulation of dopaminergic terminals in these regions drives increases in respiratory rate to initiate sniffing whereas inhibition of these terminals reduces respiratory rate. Both the firing of individual neurons and the activity of post-synaptic D1 and D2 dopamine receptor-expressing neurons are coupled with sniffing. Importantly, local antagonism of D1 and D2 receptors squelches sniffing. Ongoing work is investigating the input-output architecture of this circuit. Together, these results support a model whereby sniffing can be initiated by dopamine's actions upon specific populations of ventral striatum neurons. We propose this system likely provides a neuromodulatory means whereby motivated states signaled by dopamine release tune the occurrence and frequency of sniffing in order for animals, including perhaps humans, to acquire and appropriately process odors.

Mechanical Components Of Chemical Plume Sensing

Mitra Hartmann[1,2], Thomas Janssen[1], Neelesh Patankar[1], Shayan Heydari [3], Rajeev Jaiman[3]

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In order to efficiently track chemical plumes, animals must determine the direction of fluid flow. How do animals sense flow direction? In rats, the large mystacial vibrissae (whiskers) have been shown to play a critical role in flow-sensing behaviors. Recent results from our laboratory demonstrate that whiskers bend in the direction of airflow and then vibrate about this new deflected position. The magnitude of bending and vibration both correlate with airspeed, and vibration frequency is related to the whisker's natural frequencies. This phenomenon presents an apparent paradox: rat whiskers are so thin that vortex-induced vibrations should not occur, because the Reynolds number (Re) is well below critical. We investigated the underlying physical mechanisms driving whisker vibrations, considering both structural nonlinearities and fluid-structure interactions. Our findings indicate that vibrations result from a coupling of these two mechanisms, revealing a novel explanation for vibrations at subcritical Re. This discovery introduces new principles of vibrations at subcritical Re, with broad implications for biological systems across species. Results will be discussed in the context of animal search behaviors.

9:00 - 12:00 AM	Mangroves & Belvedere
Dance Party	