48th Annual Meeting of the Association for Chemoreception Sciences
April 22-25 2026
St. Pete Beach, FL

Printable Program & Abstracts

Wednesday, April 22, 2026

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

4:00 - 5:00 PM	Garden Courtyard
Meet and Greet	

This meet and greet hosted by the BOOST Committee will be an informal gathering to introduce our new attendees and young scholars to the AChemS community. All are welcomed to attend.

5:00 - 5:30 PM	Sawyer Key
Welcome & Awards Ceremony	

5:30 - 6:30 PM	Sawyer Key
Keynote Lecture	

5:30 **Through The Microbial Looking Glass: How Microbiomes Act As Mediators Of Animal Biology**
Kevin Kohl
University of Pittsburgh - Dept. of Biological Sciences

6:30 - 8:30 PM	South Deck/South Beach
Welcome Banquet (Ticket Required)	

8:00 - 10:00 PM	Sand Box Beach Lounge at RumFish
Trainee Campfire & Smores Meetup	

Thursday, April 23, 2026

7:30 - 9:00 AM	Pavilion/ Pavilion Lawn
Breakfast with Industry	

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We are dsm-firmenich, committed to bringing progress to life by combining what is essential, desirable, and sustainable. We operate where these forces intersect, balancing individual needs, collective requirements, and planetary demands. Our purpose is to create essential products for life, desirable choices for consumers, and more sustainable solutions for people and planet. Visit our table to learn about the range of research careers available to industry scientists in fields including receptor biology, neuroscience, microbiome & hygiene, psychophysics, materials science, chemistry, and technical product development.

Sensonics International
Sensonics International provides the medical, scientific, and industrial communities with the highest quality smell and taste tests. The Smell Identification Test™ (aka UPSIT®), the most widely used olfactory test in the world, is the ultimate test for screening organoleptic panels in the food and beverage industries, being available in over 60 languages.

8:00 - 10:00 AM	Pavilion
Poster Session I	

100 **Taste Coding From The Perspective Of A Single Taste Bud**
Syed A Uddin, Hanna Rodriguez, Thirada Boonrawd, Hojoon Lee
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Taste plays a crucial role in an animal's consumption or rejection of food. Generally, toxic and noxious substances taste bitter or sour, while nutrient-rich foods taste sweet, umami, or salty. These sensations start in the taste buds on the tongue, consisting of taste receptor cells (TRCs) innervated by axons from taste (geniculate) ganglia that carry information to the brain. Traditionally, TRC activity has been inferred indirectly by single fiber recordings of the taste fibers or by patch clamping TRCs after cell dissociation. The *in vivo* mechanisms by which individual TRCs encode and transfer this information to the nerve fibers remain unclear. To explore this, we developed a mouse model expressing a genetically encoded green fluorescent calcium indicator (GCaMP) in TRCs and taste bud nerve fibers. This model allows us to visualize the real-time activation of the TRCs and fibers in response to tastant delivery. We designed a custom 3D-printed stage to deliver tastants across the tongue of living mice. This setup allows for real-time, *in vivo* multiphoton imaging of both TRC and nerve fiber activity. Here, we will present our functional imaging results from the TRCs and their innervating fibers. Deciphering these peripheral coding mechanisms is essential for addressing taste dysfunction caused by aging, disease, and obesity.

102 **Utilizing The Htr3A-Flpo Mouse Line To Define Gustatory Neuron Innervation Of Type Iii Taste Bud Cells**
Ngozi Eze, Robin Krimm
University of Louisville

The gustatory system is a complex sensory system relying on various cell types, each expressing distinct receptor types that contribute to the perception of different taste stimuli. Type III taste bud cells transduce sour, bitter, and salt taste stimuli. In response to stimulation, Type III cells release Serotonin (5-HT), which activates Serotonin Receptor 3a- expressing nerve fibers (HTr3a-flpo). However, a definitive genetic marker for Type III associated gustatory nerve fibers has yet to be clearly defined. Here we utilized the HTr3a-flpo mice bred with reporter mice to examine the innervation patterns with Type II and Type III taste bud cells of neurons undergoing gene recombination. We found that HTr3a-flpo was expressed in (38%) of Phox2b-labeled geniculate neurons that project to the oral cavity. Furthermore, HTr3a-expressing neurons were found to innervate (94%) of fungiform taste buds. Examining the proximity between HTr3a-flpo nerve fibers and taste transducing cell types (II &III) revealed significantly greater HTr3a-flpo innervation of Type III compared to Type II taste bud cells. These findings suggest Type III taste bud cells receive preferential innervation from HTr3a-flpo nerve fibers. However, further investigation into innervation density revealed that Type III taste bud cells may inherently receive increased innervation in comparison to Type II taste bud cells, independent of neuron subtype. Perhaps the longer lifespan of Type III taste bud cells contributes to this increased innervation pattern. Consistent with this idea, using intra vital imaging we determined that newly appearing Type III cells are less well innervated than the full population. We conclude that for taste neurons the relationship between neuron subtype structure and function is complicated by plasticity.

104 **Characterization Of The Peripheral Taste Receptor Cells In Pigs**

Alison Duncan, Kathryn Medler
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Taste is a fundamental driver of food choice and consumption, yet the peripheral mechanisms underlying taste perception in humans remain poorly understood. Existing models, primarily rodents and in vitro organoid systems, have provided valuable insights but are limited in their translational relevance due to significant physiological differences and simplified cellular environments. Thus, there is a critical need for a model that more accurately reflects human gustatory physiology to advance our understanding of taste and its role in nutrition and health. We have begun investigating the possibility of using the pig (*Sus scrofa*) as a novel and translationally relevant model for studying peripheral taste receptor cells (TRCs). Pigs share significant anatomical and physiological similarities with humans and are already established models in metabolic, cardiovascular, and neurological research. Given the strong link between overconsumption of palatable foods and chronic disease, understanding how the taste system functions and adapts is essential for developing effective interventions, particularly in the pig that is more closely aligned to human physiology. Earlier anatomical and electrophysiological evidence suggests that pigs possess a highly complex taste system, yet the molecular and functional characteristics of their TRCs have not been studied. Immunohistochemical analysis is being used to define the taste cell types and identify the signaling pathways expressed in different pig taste papillae. Several known taste cell markers have been identified in the pig taste papillae but others are not expressed. These studies will advance our understanding of taste biology with the ultimate goal of enhancing strategies to address public health challenges such as obesity and Type 2 diabetes.

106 **Ace2 Is Endogenously Expressed In Taste Buds And Its Conditional Deletion From The Lingual Epithelium Results In Enhanced Neural Responses**

Emma Heisey[1], Guangkuo Dong[2], Yonggang Bao[1], Hongyan Xu[3], Lin Gan[1], Lynnette McCluskey[1]
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Angiotensin converting enzyme 2 (Ace2) is the primary receptor used by severe acute respiratory syndrome coronavirus 2 (Sars-CoV-2) to enter host cells, leading to loss of taste, smell, and chemethesis by unknown mechanisms. Following viral entry, *Ace2* is downregulated, disrupting the renin-angiotensin-aldosterone system (RAAS). Ace2 stabilizes RAAS to reduce inflammation and maintain homeostasis. While Ace2 is well characterized in other systems, its expression and biological role in the taste system remains unclear. To study this, we developed two mouse strains: a tamoxifen-inducible reporter to visualize endogenous Ace2 expression (*Ace2*$^{CE/+}$*:Rosa26-tdTomato*) and a conditional knockout (*Ace2*$^{fl/fl}$*:K14-Cre*,"Ace2 cKO") that deletes Ace2 from taste buds and surrounding epithelium. Preliminary data show robust Ace2 mRNA expression in circumvallate and anterior taste buds of wild type mice. Reporter mice reveal *Ace2* expression in keratin 8 (K8)+ taste buds, including type III taste receptor cells (TRCs) compared to corn oil controls. Neurophysiological recordings from the chorda tympani nerve revealed that male *Ace2* cKO mice had enhanced sweet and bitter responses while both sexes had increased responses to the sour stimulus, citric acid. The spatial distribution and composition of taste buds was altered in parallel with functional changes. Male *Ace2* cKO had an increase of type II TRCs, fewer type III TRCs, and taste buds were more closely spaced in the rear of the fungiform field. These results indicate that *Ace2* is endogenously expressed in taste buds and TRCs and conditional deletion alters taste bud patterning and cell composition resulting in enhanced neural responses. Ongoing studies aim to identify additional *Ace2* expressing cell types and transcriptional changes underlying functional effects.

108 **Investigating Axonal Translation At Oral Sensory Nerve Terminals Reveals A Novel Role For Fgf13 In Taste Bud Innervation And Maintenance**

Debarghya Dutta Banik, Brian Pierchala
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Taste buds are comprised of a heterogeneous population of taste receptor cells (TRCs), which are neuroepithelial in nature. TRCs die off every 2-4 weeks and are replaced by new cells. As a result, the gustatory neurons innervating these TRCs undergo constant cycles of innervation, denervation, and re-innervation. This remodeling process relies on a precise balance between signaling cues from TRCs and the surrounding lingual epithelium, as well as on the reciprocal responses of gustatory neurons. Local translation of axon-localized mRNAs is known to be critical for axon regeneration and synaptogenesis. Despite the importance of axonal translation in neuronal function, no studies have identified axonal transcripts in a physiologically and rapidly remodeling neuronal system, such as the gustatory system. To identify genes translated axonally at the taste synapse, I used an unbiased ribosomal profiling method utilizing the *Phox2b*Cre; RiboTag mouse model. To profile active translation and changes in gene expression under physiological conditions, ribosomes and associated mRNAs were isolated selectively from the axon terminals of *Phox2b*+ neurons innervating the lingual epithelium. HA-tagged, ribosome-associated RNAs were purified from lingual epithelium containing Fungiform and Circumvallate papillae. RNA-sequencing data reveal that *Fibroblast Growth Factor 13* (*Fgf13*) is highly enriched at chemosensory neuron terminals and largely absent from cell bodies. Loss of FGF13 in taste neurons leads to a severe loss of taste bud innervation and taste buds in both the CV and Fungiform papillae. These results suggest a novel role of axonal translation and axonally translated genes in the maintenance of taste bud innervation and taste buds.

110 **Roles Of Hedgehog Co-Receptor *Gas1* During Postnatal Taste Organ Development**

Gabrielle C. Audu[1], Ashlyn P. McClelland[1], Aysenur Sen[2], Michael F. McCoy[1], Archana Kumari[1]

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Hedgehog (HH) signaling is vital for the development and maintenance of taste organs; however, its role in taste organ maturation after birth remains understudied. To date, HH activity within taste buds has been primarily attributed to the ligand sonic HH. Our recent studies revealed previously underexplored expression of the HH receptor *Gas1* in embryonic, postnatal, and adult mouse taste buds of both anterior and posterior tongue regions. Studies conducted at postnatal day (P) 21 and later identified additional *Gas1* expression in the anterior tongue epithelium. Although *Gas1* loss results in craniofacial abnormalities, its specific roles in postnatal tongue maturation remain undefined. To address this gap, we used a knock-in *lacZ* reporter mouse to map *Gas1* expression and assess its role in the postnatal tongue. While *Gas1* mutant mice ($Gas1^{lacZ/lacZ}$) on a C57BL/6 background are embryonically lethal, mutants maintained on a CD1 background survive postnatally, enabling functional analysis; therefore, all experiments were conducted using the CD1 line. Consistent with embryonic observations, postnatal *Gas1* mutant tongues were significantly smaller than those of control ($Gas1^{+/+}$) or heterozygous ($Gas1^{lacZ/+}$) mice. Analysis of the anterior tongue revealed that epithelial *Gas1* expression begins by P14. Loss-of-function studies at P21 further demonstrated region-specific roles for *Gas1* during taste organ maturation. Mutants exhibited increased taste bud perimeter and a higher frequency of abnormal taste buds within anterior tongue fungiform papillae but pronounced reductions in both taste bud number and size in the posterior circumvallate papilla compared to controls and heterozygotes. In conclusion, these findings identify *Gas1* as a critical, region-specific regulator of postnatal taste bud maturation.

112 **Developing Von Ebner&Rsquo;S Glands In Embryos Are The Main Source Of $Sox10^+$ Progenitors For Taste Buds In Postnatal Mice**

Md Mamunur Rashid, Yufei Huan, Hong-Xiang Liu

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We have recently found that von Ebner's glands (vEGs) contain $Sox10^+$ progenitors for circumvallate papilla (CvP) taste buds using *Sox10-Cre* for lineage tracing and single-cell RNA sequencing. *Sox10-Cre*-traced cells comprise ~40% taste bud cells in adult mice. However, tamoxifen treatment of *Sox10-CreER^{T2}/RFP* mice after birth results in far fewer traced taste bud cells than *Sox10-Cre*. Questions remain whether $Sox10^+$ vEG cells can differentiate to taste cells *in vitro*, and when $Sox10^+$ taste bud progenitors in vEGs are generated. Using taste organoid cultures of CvP/vEG epithelial cells from *Sox10-Cre/RFP* mice, we generated organoids that contain all three types (I-III) of differentiated taste cells, and detected *Sox10-Cre/RFP* $^+$ taste cells in organoids. To define the developmental timing of $Sox10^+$ vEG progenitor contribution *in vivo*, we performed *in situ* hybridization and immunohistochemistry for identifying $Sox10^+$ vEG cells at various stages. We found that Sox10 is expressed in the emerging vEG at E16.5, and from then on in the developing and developed vEGs. Moreover, *Sox10-CreER^{T2}/RFP*-traced cells with tamoxifen during late embryogenesis (E15.5–E18.5) were initially confined to vEGs and surrounding tissues but absent in early taste buds at P1. However, embryonically traced cells were populated in taste buds in postnatal mice and progressively more abundant with age. In contrast, only sparse RFP^+ cells were detected within taste buds when tamoxifen was given to 8-week-old *Sox10-CreER^{T2}/RFP* mice. Together, these findings demonstrate that $Sox10^+$ taste bud progenitors in vEGs are produced mainly at embryonic stages, whereas $Sox10^+$ progenitors in adult vEGs contribute to taste buds to a limited extent.

Keywords: Progenitor, von Ebner's glands, Sox10, Circumvallate papilla, Taste bud.

114 **Automated 3D Tracking Of Taste Bud Cells For Morphological & Lifespan Analysis**

Brittany N. Walters, David C. Alston, Robin F. Krimm

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Taste bud cells continually die and are replaced, necessitating methods to study their dynamics. This project uses *in vivo* dual channel two-photon microscopy, performed in mice, to collect the same taste buds over time. Here, we present an analytic pipeline for 3D automated segmentation and tracking of individual taste bud cells over time. Due to the densely packed nature of cells in taste buds, manual cell segmentation and tracking are labor-intensive and inefficient. Automating these processes allows for more efficient analysis of cell morphology, spatial position, and lifespan, significantly increasing the volume of data that can be analyzed. Napari, a Python-based tool for image processing, is used to render volumetric reconstructions and generate ground-truth segmentations of individual cells. For preprocessing, we used Noise2Void, and for registration of taste bud volumes collected at successive time points, we used the Correct 3D Drift plugin in ImageJ. Concerning automated segmentation, we used a U-Net that uses transformers (SeUNet), while Ultrack tracks segmentations of individual cells over time. We have established proof of concept demonstrating that the affinity-based segmentation model performs well in sparsely populated taste buds. Based on this, we are refining the affinity model to improve performance in densely packed taste buds. Cell morphological measurements will be quantified using the MorphoLibJ plugin in ImageJ. To our knowledge, this is the first integrated tool specifically designed for automated 3D segmentation and longitudinal tracking of individual taste bud cells. It enables analysis of cell morphology and spatial position within the taste bud, measures total cell lifespan, and provides a framework for other 3D time-lapse imaging studies.

116 **Odor-Evoked Expectation In Gustatory Cortex Multiplexes Taste Identity And Lick Direction**

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In nature, animals frequently rely on non-gustatory cues to infer the identity of foods and select them for consumption. The gustatory cortex (GC) is critical for processing taste-related sensory signals, but recent evidence suggests that it also participates in cognitive functions such as expectation and decision-making. GC neurons have been found to modulate their firing rates in response to auditory, visual, somatosensory, and olfactory cues predicting the arrival of different tastes. However, it remains unknown how anticipatory GC activity conveys taste-related variables and how this activity guides ingestive behavior. To investigate these questions, we employed a two-alternative choice task in which mice learned to associate two distinct odor cues with different palatable tastes. Following odor delivery, animals licked either a left or right spout to obtain a either sucrose or monosodium glutamate (MSG) solution, respectively. To address the role of GC in this task we performed optogenetic experiments. Inhibition of GC activity during the delay between odor sampling and directional licking led to an increase in incorrect lick choices, indicating that GC contributes to consumption decisions guided by olfactory cues. Next, using high-density silicon probes, we recorded single-neuron activity in GC during two variants of the task. Analyzing firing rate changes during the delay period revealed distinct anticipatory responses to the odor cues, with preliminary evidence suggesting that both upcoming lick direction and expected taste are represented in GC anticipatory firing. Together, these findings support that GC neurons encode multiple aspects of taste expectation to guide consumption-related behavior.

118 **Functional Relevance Of Linear And Categorical Coding Units For Taste Mixture-Based Decision-Making**

Liam Lang[1,2,4], Camelia Yuejiao Zheng[1,2,3,4], Jennifer M Blackwell[1,4], Giancarlo La Camera[1,2,4], Alfredo Fontanini[1,2,3,4]

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Gustatory cortex (GC) produces time-varying activity at the population and single neuron levels that mediates food-related behaviors, including taste-based decision-making and taste discrimination learning. However, single unit functional contributions to population activity and behavior, and how such contributions evolve with learning, are underexplored. Here we address this question in mouse GC with a taste mixture-based decision-making task, *in vivo* high-density electrophysiology, and computational modeling. Mice were trained on a sucrose/NaCl mixture two-alternative choice task where the predominant mixture component cued, after a delay, the correct licking of a lateral spout. Population analyses showed GC collective activity reflected stimuli linearly during taste sampling and choices categorically before lateral lick decisions. Consistent with this, single unit tuning curve analyses revealed some neurons encoded sensory information linearly, and some encoded perceptual categories (sweet vs salty) or choices (left vs right) categorically. To probe the significance of these coding types, we built a recurrent neural network model that performed the task while reproducing the observed neural dynamics. Ablating coding units in the model showed each type, though a small fraction of the network, was required for normal dynamics and behavior, while the remaining ~60% of units were not. To assess how learning alters these units, we trained models further to match steepened psychometric functions, thus simulating neural changes underlying improving task performance. Results from this ongoing work will be presented. Our findings highlight the importance of neurons with specific response patterns in perceptual decision-making and will demonstrate how discrimination learning reshapes their contributions.

120 **Premotor Control Of Preparatory Activity In The Gustatory Cortex**

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The gustatory cortex (GC) is involved in processing cognitive signals related to a gustatory experience. In mice engaged in a delayed-response task where specific tastants guide directional licking, GC's activity has been found to progress from taste coding into preparatory coding predicting lick decisions. While preparatory and decision-related activity were consistently observed in GC, the neural mechanisms underlying these activity patterns have not been studied. The connections between GC and frontal premotor cortices involved in guiding goal-directed actions provide a putative source of preparatory signals to GC. 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, delayed-response task where tastants instructed directional licking. We first anatomically identified direct ALM inputs in GC using AAV-based tracing approaches. We then performed simultaneous electrophysiological recordings during task performance and found preparatory activity emerged earlier in ALM than in GC. 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 frontal premotor inputs significantly contribute to GC preparatory activity during taste-guided decision making.

122 **Olfactory Bulb Gamma Oscillations May Represent A Valence Scaffold For The Next Sniff**

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Predictive coding frameworks propose that sensory systems continuously generate top-down predictions that are compared with incoming sensory input. For the visual and auditory domains, gamma-band activity is considered to mainly convey bottom-up sensory evidence, while beta-band activity is thought to reflect top-down predictive signals. Whether the human olfactory system operates under a similar regime remains largely unknown. Building on previous findings demonstrating bidirectional, valence-related communication between the olfactory bulb (OB) and piriform cortex (PC), we recorded activity from both regions simultaneously using the electrobulbogram (EBG) method in 32 healthy participants. Odors varying in valence were presented across two consecutive sniffs, with valence switched in 20% of trials to create a sniff-by-sniff oddball paradigm. When odor valence was repeated, OB gamma activity increased during the second sniff, consistent with a refinement of the sensory representation. However, when odor valence changed between sniffs, this gamma enhancement disappeared, and OB gamma resetted to first-sniff levels. This pattern indicates that OB gamma activity reflects a refinement process that depends on the stability of sensory input across sniffs. These findings suggest that the human olfactory system engages gamma-mediated updating mechanisms and may participate in a broader predictive-coding architecture, although its implementation may differ from what is commonly demonstrated in vision and audition.

124 **Assessing The Morphological And Electrophysiological Substrates Of Experience-Dependent Plasticity In Accessory Olfactory Bulb Interneurons**

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Social behaviors in terrestrial mammals are guided by conspecific and heterospecific chemosensory cues. In rodents, these cues are detected by the accessory olfactory system (AOS), in which the accessory olfactory bulb (AOB) serves as the first dedicated circuit for chemosensory processing. Within the AOB, inhibitory internal granule cells (IGCs) form reciprocal dendrodendritic synapses with mitral cells (MCs) and regulate circuit excitability and network dynamics. Previous work has demonstrated that a subset of IGCs selectively expresses the immediate-early gene *Arc* following social encounters and exhibit persistent increases in intrinsic excitability. However, whether these experience-activated neurons also undergo coordinated structural remodeling remains unknown. Here, we examined the morphological and intrinsic physiological properties of Arc-expressing IGCs using transgenic mice that enable permanent Arc-dependent labeling (ArcTRAP). Using a combination of whole-cell patch-clamp recording, biocytin filling, and multiphoton imaging, we found that many ArcTRAP+ IGCs exhibit increased dendritic length and elevated dendritic spine density relative to neighboring ArcTRAP- neurons, consistent with an enhanced capacity for synaptic integration. In parallel, ArcTRAP+ IGCs display increased intrinsic excitability, replicating prior observations. Together, these data suggest that experience-activated inhibitory interneurons undergo coordinated functional and structural plasticity, potentially strengthening inhibitory control within AOB circuits. By linking activity-dependent gene expression to persistent changes in neuronal excitability and morphology, this work identifies a candidate cellular substrate through which social experience may shape AOB circuit dynamics and long-term chemosensory processing.

126 **Measuring Human Olfactory Bulb Gamma On The Single Breath Level**

Adam Dede[1], Qiohan Yang[1], Andrew Sheriff[1], Naelly Arriaga[1], Aditi Agarwal[2], Sajel Peters[2], Gregory Lane[1], Justin Morgenthaler[1], Christina Zelano[1], Bruce Tan[2]

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The olfactory bulb (OB) is a canonical generator of respiration-locked network rhythms, including multiple gamma sub-bands. Here we characterize a continuously expressed low/slow-gamma oscillation in the human OB in awake humans at single-breath resolution and test how its coupling to respiration depends on attentional set. We recorded OB-proximal field potentials using minimally invasive intranasal stereo-electrodes positioned immediately beneath the cribriform plate, with electrode location confirmed by CT in every participant. Across individuals, low-gamma peak frequency varied between individuals yet was highly stable within individuals across breaths and across sessions. On each breath, both gamma amplitude and instantaneous frequency were systematically modulated by respiratory phase, demonstrating that gamma is not merely stimulus-evoked but an ongoing rhythm embedded within the breathing cycle. Critically, the phase of maximal gamma amplitude depended on behavioral context: during passive nasal breathing while listening to an audiobook, gamma was strongest during exhalation; after mindfulness meditation instructions that encouraged interoceptive attention to breathing, the preferred phase became bimodal, concentrating near the inhale–exhale transition and the end of exhalation, with reduced expression in mid-exhalation. These findings establish single-breath gamma as a robust, individual-specific signature in human OB and reveal that attention dynamically reconfigures respiration–gamma coupling, providing a mechanistic bridge between breathing, sensory circuits, and cognitive state.

128 **Dynamics Of Neural Oscillations In The Olfactory Bulb Related To Task Demands**

Andrew Sheriff[1], Gregory Lane[1], Qiaohan Yang[1], Adam Dede[1], Naelly Arriaga[1], Bruce K. Tan[2], Leslie M.

Kay[3,4], Christina Zelano[1]
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Olfactory system dynamics change depending on behavioral state and can be measured via neural oscillations, for example olfactory bulb (OB) gamma power is generally enhanced during wakefulness compared to sleep. More specifically, OB gamma is enhanced during difficult learned associations of very similar odors, and beta oscillations emerge during olfactory learning, potentially serving different mechanisms. Using single-trial-precision recordings of OB local field potentials (LFPs), we explored whether these neural oscillations appear in the human OB during an odor discrimination task. A pair of odors (ketones or alcohols) that were very similar to each other (fine discrimination), but more noticeably different across pairs (coarse discrimination), were used for this task. In each trial, participants (n=6) were presented a pair of odors (fine, coarse, or same), chosen randomly among the 3 conditions, and participants then indicated whether the pair of odors were the same or different. Preliminary data shows significant beta and gamma oscillations emerging during sniffs of odors ($p<0.05$, permutation test against pre-sniff baseline, FDR-corrected), in line with those seen during olfactory learning tasks in rodents. Dynamics of these neural oscillations during sniffs will be related to task performance and discrimination difficulty, and task periods between sniffs will be analyzed for top-down signals, hypothesized to emerge in low gamma (30–60 Hz) and beta (15–28 Hz) bands.

130 **High-Resolution Mri Of Laminar Structures In The Human Olfactory Bulb In Vivo**

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The olfactory bulb (OB) consists of six distinct layers. The axonal projections from the OSNs converge in the olfactory glomeruli contained in OB layer II, the glomerular layer (GL), from which it synapses onto neurons and interneurons in subsequent layers. High resolution MRI of *ex vivo* human OB specimen has been attempted previously at 3T. However, the image quality was not clinically readable, and the duration of MRI scan (100 minutes) was prohibitory for clinical exams. Here, we show that optimized MRI scans performed on high-field (7T) human MRI systmes can image structural laminar organization of the human OB *in vivo*. With a spatial resolution of 0.4 mm and scan time of 12 minutes, laminar structures in the OB can be visualized in healthy human subjects. Laminar structures with signal intensities corresponding to OB Layers I, II, III and VI in *ex vivo* images can be clearly identified in our *in vivo* images. The width of *in vivo* OB was wider than *ex vivo* OB specimen (~3.4mm vs. ~2.1mm). Importantly, the OB Layer II (glomerular, GL) can be segmented in the *in vivo* images with an approximate width of 0.6 mm.

132 **Beyond Bold: Unlocking Human Olfactory Bulb Function With Asl Perfusion Imaging**

Ludwig Sichen Zhao[1,2], Manuel Taso[3], M. Dylan Tisdall[3], John A. Detre[2,3], Jay A. Gottfried[2,4]
[1]Department of Bioengineering, School of Engineering and Applied Science, University of Pennsylvania, Philadelphia, PA, United States, [2]Department of Neurology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States, [3]Department of Radiology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States, [4]Department of Psychology, School of Arts and Sciences, University of Pennsylvania, Philadelphia, PA, United States

Olfactory processing begins in the olfactory bulb (OB), where afferent inputs are organized and transformed into neural representations. Moreover, OB dysfunction is implicated as an early feature of multiple neurodegenerative diseases. Despite extensive mechanistic work in rodents and non-human primates, in vivo study of the human OB remains limited due to constraints on imaging techniques. In particular, blood-oxygen-level-dependent (BOLD) functional MRI (fMRI) is widely used in human neuroimaging but is poorly suited for the OB because its proximity to the air-tissue interface near the sinuses induces severe susceptibility artifacts and signal dropout. Arterial spin labeling (ASL) offers a promising alternative by quantifying blood flow (perfusion) as a direct readout of neurovascular coupling. In prior work, we demonstrated that our ASL approach improves sensitivity in high susceptibility regions, motivating its application to olfactory structures. However, ASL in small targets, such as the OB, remains challenging due to low signal-to-noise ratio, often requiring long acquisitions and limiting spatial and temporal resolution.
Here, we developed and optimized an ASL protocol to detect perfusion signals within the OB and paired it with a newly developed denoising method to improve spatiotemporal resolution. We demonstrate reliable OB blood-flow measurements within a clinically practical scan time and characterize the resting-state network in the human OB. Together, these results establish ASL as a viable approach for probing human olfactory regions where BOLD fMRI is constrained, advancing functional and translational studies of the human OB and olfactory system.

134 **Enhanced Multisensory Integration In The Olfactory Bulb Of Astyanax Mexicanus**

Evan Lloyd, Anna Koga, Sophia Ford, Douglas Storace
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Here we examined whether the olfactory system of the blind Mexican cavefish (*Astyanax mexicanus*) exhibits

any compensatory adaptations in comparison to the surface morph. Cavefish had larger synaptic input from the olfactory epithelium (OE) to the olfactory bulb (OB), which occurred uniformly across all glomeruli, and increased numbers of dopamine and calretinin-expressing neurons within the OB. Notably, the increase in cavefish calretinin neurons could not be explained as a simple increase in brain volume. Ca2+ imaging of the OB in response to a panel of odors revealed chemotopic patterns that were relatively conserved across both morphs. Surprisingly, we observed that the medial dorsal bulb responded to our water control stimulus in both morphs, which reflects a mechanosensitive response to changes in water flow, but with greater numbers in cavefish. We confirmed that both morphs had olfactory sensory neurons that express the mechanosensitive ion channel Piezo2 in the OE, although cavefish had significantly more neurons expressing Piezo2. Therefore, cavefish exhibit enhanced multisensory integration beginning at the first stage of olfactory sensory processing.

136 **Receptor-Defined Lateral Inhibition In The Mammalian Olfactory Bulb**

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Lateral inhibition plays a key role in shaping olfactory bulb output, yet its functional organization remains unclear. Inhibitory connections may be selectively structured by receptor identity or randomly distributed across the bulb, but testing these alternatives has been limited by the difficulty of mapping inhibitory inputs onto receptor-defined principal output neurons. To address this, we generated three odorant receptor (OR) tagged mouse lines in which olfactory sensory neurons (OSNs) expressing a specific OR co-express the fluorescent marker mKate2. These lines targeted one class I OR (Or52h2) and two class II ORs (Or10g9b and Or1ad1) and were crossed with mice expressing genetically encoded calcium indicators in either OSNs or mitral/tufted (MT) cells. We presented large odorant panels (40-50 odorants) to awake mice to characterize OSN and MT tuft tuning of tagged glomeruli. Excitatory tuning sharpened post-synaptically, and odorant-evoked suppressive responses also emerged. Odorants that suppressed Or52h2 dendritic tufts also suppressed daughter MT cell somata, indicating that suppressive glomerular signals reflect inhibition of olfactory bulb output. Notably, suppressive response spectra were stereotyped across animals, and odorants that activated class II OSNs did not suppress Or52h2 MT cells. This result appeared to generalize to other class I glomeruli. Moreover, suppression was overall less prevalent in MT tufts associated with the two class II glomeruli compared to the class I glomerulus. Together, these results support a receptor-defined rather than random inhibitory architecture and suggest that lateral inhibition in the olfactory bulb is heterogeneous across OR classes.

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

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Sensory perception is shaped by internal states, but the integration of intrinsic and extrinsic signals by sensory circuits is poorly understood. We are using the mouse olfactory system to study how non-sensory cues regulate information processing in sensory circuits. We hypothesize that local dopamine neurons (DANs) in the olfactory bulb (OB) mediate state- and task-dependent changes in odor encoding. Also known as superficial short axon cells (sSACs), OB DANs are well-positioned to orchestrate fast and reversible changes in odor-evoked activity in the OB as they (1) link up to 50 glomeruli, enabling interglomerular communication, (2) modulate the activity of mitral and tufted cells (MTCs), the principal neurons of the OB, via D1, D2 and GABAA receptors, and (3) receive direct inputs from the basal forebrain, a major source of top-down regulation in the brain. Using two-photon imaging of the OB through a chronic cranial window, we are quantifying the spatial-temporal dynamics of OB DAN activity in vivo, as mice are passively exposed to odors or while mice perform odor discrimination tasks. Preliminary experiments targeting the expression of GCaMP8f and JEDI-2P to OB DANs in TH-Cre mice suggest that OB DAN activity is heterogeneous across glomeruli and odor-dependent. In vivo imaging of the DA sensors GRAB-gDA3h and dLight1.3b also supports heterogeneous DA release across and within glomeruli. On-going experiments will reveal the relationship between DAN activity, DA release and MTC activity in the OB of awake vs anesthetized mice, and in behaving mice before and after chemogenetic modulation of OB DANs. Our results will help us better understand the neuromodulation of olfaction and the neural circuits behind flexible stimulus encoding.

140 **Defining Cd11B-Dependent Glial Phagocytosis And Gene Expression Changes After Olfactory Injury**

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Integrin CD11b, or complement receptor 3, is utilized by myeloid cells to govern phagocytosis and cellular movement to sites of infection or injury. Recognizing over 40 ligands, this integrin plays various immune roles throughout the body. In the olfactory system, CD11b is primarily expressed by microglia. Our lab uses a methimazole-induced olfactory injury model to ablate all olfactory sensory neurons and observe the glial response in both wild-type and global CD11b-deficient mouse models. Previously, our lab saw significant delays in functional recovery and changes in Iba1 expression in CD11b-deficient mice following methimazole injection. To further explore changes in this system, we injected methimazole at post-natal day 7 and collected olfactory bulbs at 3, 7, 14, and 21 days post-injection to quantify phagocytic and gene expression changes by flow cytometry and qPCR, respectively. We implemented a newly developed fluorescent cell sorting method based on marker proteins and the presence of internalized axonal debris and quantified the phagocytic activity of microglia and OECs in wild-type and CD11b-deficient mice. Expression changes in phagocytic markers, inflammatory mediators, and neuroprotective intermediates were quantified by qPCR to elucidate pathway alterations in the olfactory bulb that may contribute to the delays in functional olfactory recovery seen previously in this model.

142 **Noggin Bonks And Neurogenesis: Alterations In Olfactory Bulb Adult Neurogenesis Following A Mouse Model Of Tbi**

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Traumatic Brain Injuries (TBIs) produce a variety of symptoms and complications in humans and often result in extensive cell death in the brain. In adulthood, neurogenesis, predominantly occurs in the Hippocampus and Subventricular Zone (SVZ). SVZ neural progenitors migrate along the Rostral Migration Stream (RMS) to the Olfactory Bulb (OB) where they become interneurons. Following TBI, there is a spike in neurogenesis in the hippocampus but little is known about the impacts to olfactory bulb neurogenesis. To investigate the location of adult born cells following a TBI, we used a controlled cortical impact (CCI) mouse model of TBI followed by cell proliferation tracking using BrdU pulse labeling at 7-10 days post-injury. We also found surprising increases in adult-born cells on the ipsilateral side of the brain, particularly near the injury site, in the peri-infarct cortex, dentate gyrus and ipsilateral thalamus. immunohistochemistry revealed an astrocytic phenotype of most newborn cells. At the same time, we found a decrease in adult-born neurons in the OB. To determine whether neurons that successfully reach the OB were typical or abnormal as a result of being born and migrating under pathological and inflammatory conditions, we injected Lentivirus into the SVZ followed by CCI, Sham surgery or no surgery. This demonstrated that neural progenitors were not being diverted from the SVZ. Furthermore, lentivirus labeled adult born neurons in the OB of CCI mice appeared qualitatively morphologically abnormal, with less complex arbors. This appears true of mature neurons, no longer expressing DCX, an immature neuronal marker, and of immature viral labeled cells colabeled with DCX.

144 **Using Targeted Recombination In Active Populations (Trap), 2-Photon Calcium Imaging, And Metabolic Monitoring To Investigate The Effect Of Administration Of The Glucagon-Like Peptide 1 (Glp-1) Agonist Semaglutide In Mice.**

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Glucagon-like peptide 1 (GLP-1) agonists provide strong therapeutic use to combat obesity, among a host of additional health-related benefits. Given that there is a GLP-1 signaling microcircuit in the olfactory bulb (OB), whose activation elicits a multiphasic response shaping mitral/tufted cell (M/TC) firing patterns, we examined the effect of semaglutide (sema) administration in mice. Fos2A-iCreER mice (TRAP2) mice were intraperitoneally injected with sema causing M/TC and granule (GCs) cells to be activated (TRAPPED), as well as anticipated neurons in the lateral hypothalamus (LH). FL-sema was used to map and determine access of the drug to the OB and the LH within 30 m – 4h. Specificity of binding was confirmed by substituting mice with targeted deletion of the GLP-1R. Next, mice lines in which odorant receptor (Olfr) 649 expressing mKate2 reporter were crossed with mice expressing genetically-encoded calcium reporter GCamp6f in M/TCs. These mice were maintained on control (CF) or moderately-high fat (MHF) diets, daily administered sema for one month or were isocalorically-restricted to the consumption of the drug-treated animal. Mice were surgically implanted with a cranial window to probe glomerular activity with valeric acid using an awake paradigm. Metabolically, sema caused abrupt weight loss that was proportionally congruent in both CF- and MHF-maintained mice. Weight loss that was driven by isocaloric restriction was gradual and stabilized to pre-restriction values when mice were removed from diet restriction, unlike sema-treated mice that rebounded to heavier body weights once removed from drug treatment. We are continuing analysis of glomerular activation to determine if it might be modulated by body weight changes induced by activation of GLP-1 signaling circuits.

146 **A Quantitative Perceptual Framework For ReconstructiNg Complex Food Odors**

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Odor perception plays a central role in food preferences, yet we lack a quantitative framework for understanding how complex food odors emerge from molecular mixtures. Odor mixtures have been reported to exhibit qualities distinct from their individual components, suggesting that interactions between odorants dominate mixture perception. However, linear models that assume independent and additive perceptual contributions from component molecules have performed surprisingly well at predicting odor mixture character in human behavioral studies using mixtures of up to 10 components. To test how well linear models can reproduce complex food percepts, we collected descriptive ratings for 24 foods alongside their published Sensomics-based reconstructions (GC-MS analysis followed by sensory testing). Using greedy search within a linear perceptual framework, we iteratively selected components from a database of ~700 individual stimuli to identify component mixtures minimizing perceptual distance to each target food and best approximating each food's sensory profile. For 18 of 24 foods, these perceptually-optimized mixtures matched the target food more closely than the Sensomics reconstructions, despite using no information about the foods' chemical composition. These results demonstrate that odor components combine predictably even in complex foods, extending the validity of linear

mixture models from simple laboratory mixtures to real food systems. A perceptual framework for olfactory mixture design offers a complementary approach to analytical methods, enabling food odor reconstruction from any available ingredient library.

148 **Behavioral State And Ethological Salience Shape Hdb Cholinergic Activity During Naturalistic Olfactory Exploration**

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Basal forebrain cholinergic signaling is widely implicated in attention, arousal, and sensory processing. Studies using operant paradigms demonstrate rapid cholinergic fluctuations during task engagement, yet these approaches primarily capture population-level neuromodulatory signals driven by explicit cues and reward contingencies. Consequently, how identified cholinergic neurons in the horizontal limb of the diagonal band of Broca (HDB) are engaged during self-directed olfactory exploration outside trained behavioral frameworks remains poorly understood.To address this gap, we expressed GCaMP8f in cholinergic neurons of the HDB in ChAT-Cre mice and performed miniscope imaging as animals freely explored an environment containing social or non-social odors across multiple days. Rather than aligning neural activity to odor onset or task epochs, we used ethogram-based annotation to define investigative bouts, behavioral transitions, and non-investigatory states during natural exploration.We find that HDB cholinergic activity is structured by behavioral engagement, with elevated activity during investigative bouts and transitions into investigation. During odor sampling, HDB populations exhibit investigation-locked responses and odor-category-dependent ensemble coordination that dissociates familiarity from ethological salience. Familiar stimuli, such as bedding, elicited strong and coordinated responses, while response magnitude declined across days with environmental familiarization but remained elevated during re-engagement. Together, these findings indicate that HDB cholinergic activity during olfactory behavior reflects state-dependent modulation shaped by self-directed investigative structure rather than stimulus identity or task demands alone.

150 **Choice Signals Emerge In Mouse Piriform Cortex During Delayed Olfactory Decision Making**

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Piriform cortex (PC) multiplexes respiration-entrained activity with odor identity and intensity, but its role in encoding choice during odor-guided decisions remains debated. Prior work relied on go/no-go tasks where sensory evidence, choice, and movement are coupled. To dissociate these factors, we recorded respiration and PC spiking from large ensembles of neurons in mice performing a delayed 2-alternative forced-choice task. Stimuli were two pure odors and mixtures across four concentrations (+Limonene/-Limonene: 0/100, 30/70, 70/30, 100/0) and mice chose left for the first two and right otherwise. This task separates graded sensory signals tracking odor concentration from categorical signals tracking choice. To demix sensory (respiratory and odor-related) and choice signals, we fit generalized linear models incorporating respiration, odor features, and choice. PC neurons showed diverse coding, including units whose firing rate increased linearly with odor concentration and units with all-or-nothing categorical responses. Some neurons showed linear encoding early after odor onset and switched to categorical, choice-predictive coding later in the delay. To probe a mechanism for categorical activity, we trained a recurrent neural network with PC-inspired cell-types and connectivity on the same task. The model reproduced linear sensory and categorical choice encoding. Suppressing recurrent excitation impaired performance and reduced categorical activity, suggesting that recurrent circuitry promotes choice coding. We are testing this in vivo by expressing tetanus toxin light chain in PC pyramidal neurons while monitoring behavior and neural dynamics. Together, these results show that choice signals emerge in PC during delayed olfactory decisions and may be facilitated by local recurrent circuitry.

152 **Time-Course Of Odor Coding In The Human Brain - A Single-Neuron Perspective**

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Odor information arising from the olfactory bulb is projected in parallel to the piriform cortex, amygdala, entorhinal cortex, and other sub-regions of the primary olfactory cortex. These brain areas, which receive direct monosynaptic input from the olfactory bulb, are highly interconnected and functionally linked to higher-order regions, including the hippocampus. However, the precise latency and temporal evolution of odor coding within and across these regions in the human brain remain largely unexplored. To address this, we conducted rare single-neuron recordings in epilepsy patients undergoing invasive intracranial seizure monitoring with Behnke-Fried electrodes. We recorded neuronal activity from the piriform cortex, amygdala, entorhinal cortex, hippocampus, and parahippocampal cortex (1011 units across 15 sessions) during an odor identification task in which short, 200-ms odor pulses were delivered via a computer-controlled olfactometer. Odors were delivered using a closed-loop system at consistent phases of the inhalation cycle to ensure temporal precision. Preliminary results show that neurons in the piriform cortex exhibit the earliest and strongest odor responses and that a higher proportion of piriform neurons are modulated by odors compared to the other regions. At the population level, we observed both rapid and sustained odor coding in the human olfactory network lasting ~7 seconds after odor presentation. Together, these initial findings demonstrate rapid and precise processing of complex odors by neurons in human olfactory network, laying the foundation for exploring interregional transmission and temporal dynamics in the human brain.

154 **Population-Level Variation In Olfactory Receptor Tuning In *Drosophila Mojavensis***

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Host plant associated divergence is a major driver of ecological speciation. In herbivorous insects, adaptation to distinct plant hosts can shift insect behavioral preference and sensitivity of the peripheral olfactory nervous system to plant chemical cues. These cues are detected by olfactory sensory neurons (OSNs) expressing odorant receptor genes. *Drosophila mojavensis* is a powerful insect system for studying incipient speciation, because its four geographically isolated populations each specialize on a chemically distinct cactus host. Here, we examine how OSN tuning differs between two of these populations, Catalina and Mojave. Using single sensillum recordings, we quantified OSN responses across 10 antennal sensilla to 39 cactus-associated odorants across an eight-point concentration gradient. This generated a high-resolution dataset capturing the magnitudes of population specific responses. Results revealed that while many OSNs show conserved tuning, a subset display significant divergence to multiple odorants and concentrations. For a subset of odorant-OSN combinations, Mojave population exhibits an increased sensitivity to cactus- associated odorants at intermediate concentrations (10^{-5} -10^{-3}) consistent with horizontal shifts in tuning curves. The observed population-specific shifts in OSN dose-response curves highlight divergence in peripheral olfactory coding between the two populations. These results provide a framework for identifying OSNs that show population specific differences in tuning that are likely contributors to odor-guided behavioral differences in *D. mojavensis*.

158 **Accessory Olfactory Bulb Mitral Cell Representations Of Naturalistic Social Odors Across Stimulus Intensity, Sex, And Cellular Compartments**

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The mammalian accessory olfactory system (AOS) detects secreted, fluid-borne social chemosensory cues. These cues are sensed by sensory neurons in the vomeronasal organ (VNO), where they evoke activity that is transmitted directly to mitral cells (MCs), the principal output neurons of the accessory olfactory bulb (AOB). Within the AOB, MC responses are further shaped by local inhibitory circuits, generating neural representations that modulate important social centers downstream. Despite their central role, key aspects of MC function remain unclear, including how MCs encode stimulus intensity, whether sensory representations differ between sexes, how cellular anatomy shapes stimuli tuning, and whether there exists a spatial organization of the MCs responses within the AOB depending on the sensory input type. To address these gaps, we measured AOB MC calcium responses to a panel of naturalistic urine stimuli using an *ex vivo* AOS preparation that preserves functional connectivity between the VNO and AOB. Using virally mediated GCaMP6f expression and two-photon imaging, we recorded MC activity in adult male and female Pcdh21-Cre mice while stimulating the VNO across multiple stimulus concentrations. We combined small-field single-plane imaging with wide-field volumetric imaging to compare tuning properties across distinct MC compartments, including glomerular tufts, primary dendrites, and cell bodies. Together, this work advances our understanding of how AOB mitral cells encode socially relevant chemosensory information and organize their neural representations within the AOB, and establishes a foundation for future studies examining how experience-dependent plasticity in the AOS shapes neural activity patterns that support behavioral flexibility.

160 **Examining The Neural Representations Underlying Odor-Guided Behavior In Humans**

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The process of generating adaptive behavior from olfactory sensory input involves a range of brain regions, including the primary olfactory cortex (PCX), ventral prefrontal cortex (PFC) and mediodorsal thalamus (MDT). Recent animal studies demonstrate that MDT both encodes information about specific odorants, and mediates connectivity with sensory and prefrontal cortices to guide behavior. However, the mechanisms by which these regions guide odor-guided behavior in humans remain unclear. Here we designed an experiment in which human participants perform an odor-guided learning task while undergoing ultra-high field fMRI. On each trial of the task, participants receive one of three distinct odors, and then make one of two possible responses to receive a monetary reward. Critically, in some trial blocks the rewarded response is the same regardless of odor identity, and in other blocks identity determines the correct response. This experimental design allows us to test the primary hypothesis that ensemble MDT activity preferentially encodes information about odor identity when identity is relevant for making a decision. We further hypothesize that activity in the PCX primarily represents odor identity, while patterns of PFC activity reflect decision outcome. Pilot behavioral results (n=15) demonstrate that participants make highly accurate choices regardless of block type, and that residual differences in odor pleasantness and intensity do not affect performance. Analysis of our collected fMRI data employs multivariate pattern-based techniques to characterize how the balance of olfactory sensory and behavioral task variables are represented in olfactory sensory cortex, MDT, and prefrontal cortex to support learning.

162 **Evidence That Interglomerular Inhibition Generates Non-Monotonic Concentration-Response Relationships In Mitral/Tufted Glomeruli In The Mouse Olfactory Bulb**

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Animals can recognize and discriminate between different odors and the same odor over a range of concentrations. Processing within the mouse olfactory bulb (OB) may be involved, yet the underlying neural mechanisms remain unclear. Each olfactory receptor neuron (ORN) type maps to the olfactory bulb in olfactory receptor specific channels called glomeruli where they connect with the dendrites of mitral/tufted cells (MTCs), which project their axons to the rest of the brain. Differences between input and output define the functions carried out by a brain area. Using *in vivo* dual-color 2-photon calcium imaging from the ORNs and MTCs innervating the same glomeruli in the mouse OB, we identified that monotonically rising concentration-relationships in ORNs were transformed into different MTC response types that included monotonic and non-monotonic concentration-response relationships. Mathematical modeling was used to demonstrate that one of the non-monotonic response types is consistent with a form of interglomerular processing. We propose that the transformation from exclusively monotonic ORNs to a combination of monotonic and non-monotonic MTCs would facilitate odor discrimination and the ability to achieve concentration-invariant odor perception.

164 **Evolutionary Diversity And Function Of Odorant Receptors In Birds**

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An incredible variety of chemicals are perceived as smell by animals. To detect this vast range of volatiles, odorant receptors (ORs) have diversified into one of the largest gene families in vertebrates; for example, many mammals have over 1,000 OR genes. Birds, with over 10,000 extant species, inhabit nearly all land environments and exhibit diverse breeding and foraging behaviors yet were long thought to make limited use of olfactory signals. Here, we used genomic and molecular approaches to demonstrate the relevance of the avian olfactory system. We show that, like mammals, bird genomes often contain hundreds – or in some cases, thousands – of intact ORs, including the nocturnal kiwi (*Apteryx manetllii*), which possesses the largest number of ORs known from any animal. The majority of avian ORs belong to a bird-specific expansion known as gamma-c ORs. We found that this expansion was characterized by extensive gene conversion leading to mosaic open reading frames with diverse regions interspersed with regions nearly identical in nucleotide sequence. We show that avian ORs are expressed in olfactory sensory neurons and respond to specific odors *in vitro* and *in vivo*. Notably we identify for the first time ligands for avian ORs documenting both unique function in gamma-c ORs and shared function with a deeply divergent mammal OR. Our findings highlight commonalities between mammals and birds in olfactory system function but also reveal a unique evolutionary feature: the widespread role of gene conversion shaping the majority of bird ORs. Our results challenge prior assumptions and underscore the importance of olfaction in the life history of birds.

166 **Engineering Insect Odorant Receptors Towards Volatiles Of Interest**

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Odorant Receptors (ORs) are sensitive chemical receptors that can respond to a diverse array of volatile chemicals. In insects, ORs are ion channels, containing four, seven-transmembrane domain subunits capable of mixing and matching. Most insects have a highly conserved OR co-receptor. The ORco does not respond to ligands itself but is key for conferring stability by mixing with diversive ORx subunits that respond to volatile compounds. The heterotetramers formed by this combination are the backbone of olfaction in insects. However, not all insects have an ORco, and one notable exception is the Jumping Bristletail (*Machilis hrabei). M. hrabei* was found to be quite a basal insect, only containing five ORs with no ORco. Through previous work, two of these ORs show significant expression and function in modern cell culture-based systems. Additionally, the structure of one of these ORs, MhOR5, was experimentally elucidated, providing the most accurate data for chemical interactions inside the receptor. Therefore, our work has used MhOR5 as a backbone to understand the ligand binding properties of insect ORs. We created a panel of diverse, human-relevant volatile chemicals and tested them against MhOR5 and an array of mutants to build a better understanding of the contribution of binding pocket residues towards ligand binding and receptor activation. Furthermore, we are engineering a system to mutate and characterize MhOR5 to specific ligands in a manner that creates combinatorial mutants in a non-biased, high-throughput approach. This work is the beginning of an understanding of how ligands selectively activate insect ORs, and what structural features contribute to binding and activation. This data will be key in the engineering of ORs towards volatiles of human interest.

168 **How Local And Lateral Inhibition Shape The Odorant Response Function In The Olfactory Bulb**

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Coding of olfactory signals at the level of the olfactory bulb involves both intraglomerular and interglomerular inhibition. We use mathematical modeling to understand how each of these processes may contribute to mitral/tufted cell (MTC) output signals. In particular, we seek to understand how the two forms of inhibition contribute to non-monotonic responses of MTCs over a range of odorant concentrations (see poster by Leong et al.). We perform an analysis of a simple mathematical model to demonstrate how differences in the olfactory

receptor neuron (ORN) odorant response functions over a range of concentrations map into different types of MTC response functions. We also highlight how the two forms of inhibition affect this mapping and achieve this via precisely characterizing the ORN parameter space using bifurcation theory. We show that parameters affecting intraglomerular inhibition are mathematically separable from those affecting the ORN response and interglomerular inhibition; thus, they have independent effects on the MTC response. This is true regardless of the structure of the interglomerular inhibitory network, which is currently unknown.

170 **Odorant Receptor Antagonism As A Mechanistic Basis For Malodor Counteraction**

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Malodors, such as moldy or earthy notes on fabrics, present a persistent consumer challenge. Reduction of malodor perception is traditionally attributed to perceptual masking, yet increasing evidence suggests a mechanism by which this can occur is via antagonism of odorant receptors (ORs). Here, we evaluate this relationship by testing the hypothesis that OR inhibition can predict malodor perceived intensity in human sensory evaluations across multiple malodors. An expert perfumer evaluated binary mixtures of several malodors with panels of odorants and rated their effectiveness at counteracting malodor perception. In parallel, we quantified the inhibitory effects of these compounds on the corresponding ORs using a unified inhibition index derived from *in vitro* heterologous assay measurements. Our results provide direct evidence that OR inhibition contributes to malodor counteraction and demonstrate that receptor-level metrics can predict sensory counteraction performance. This work establishes a mechanistic framework for malodor control and supports OR inhibition as a general design principle for next-generation fragrance and flavor development.

172 **Subthreshold Modulation Of Varietal Identification By 1,1,6-Trimethyl-1,2-Dihydronaphthalene Under Controlled Olfactory Delivery**

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Context: Odor mixture perception is shaped by nonlinear interactions among component odorants, such that compounds below explicit recognition thresholds may influence categorical judgments. This study examined whether 1,1,6-trimethyl-1,2-dihydronaphthalene (TDN), a compound associated with Riesling aroma, modulates varietal identification when added to Chardonnay at sub- and near-threshold concentrations. Method: Using a computer-controlled sniff olfactometer, approximately 15 participants were tested in a forced-choice double blind screening followed by a perceptual task without explicit training or feedback. Screening assessed basic varietal discrimination ability under identical delivery conditions. In the main task, Chardonnay stimuli were systematically supplemented with nine concentrations of 1,1,6-trimethyl-1,2-dihydronaphthalene (TDN), spanning subthreshold to suprathreshold levels. TDN was prepared in a polyethylene glycol (PEG 400) carrier and diluted in with water to ensure precise concentration control and consistent odor delivery. On each trial, participants performed a binary varietal identification judgment (“Riesling” vs. “Not Riesling”). Choice behavior, confidence, and reaction time were recorded to evaluate dose-dependent shifts in perceptual categorization. Results: When the added TDN concentration in the headspace of no-oak Chardonnay wine was at or below its threshold subjects more frequently identified it as Riesling than not. Above the TDN threshold the chardonnay headspace was not identified as “not-Riesling” but identified as “Petrol” smell. TDN in Riesling seems to act as a “silent note” as described by Xu in 2023.

174 **The Aob Mitral Cells Provide A Cellular Basis For The Independent Encoding Of Conspecific Sex**

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The mouse accessory olfactory bulb (AOB) processes chemosensory information carried by conspecific cues. The accessory olfactory system (AOS) is crucial for sex recognition and individual recognition. In the AOB, the sex and strain of conspecific cues are encoded at the population level, and individual AOB neurons respond to specific, and often complex, combinations of sex and strain. However, it is unclear whether and how conspecific sex is encoded independent of their strain by the AOB circuit. Here, we study the encoding of conspecific males by the AOB mitral cells in response to urine from a panel of inbred mouse strains. Using two-photon calcium imaging of the AOB in an ex-vivo “hemi-head” preparation, we report a functional type of “pan-male” AOB mitral cells that detects males regardless of their strain. We also identified several other functional types of AOB mitral cells, which have varying combinatorial patterns of activity in response to conspecifics. Interestingly, the “pan-male” mitral cell type was found more frequently in the female AOB than in the male AOB. Taken together, the evidence suggests that the AOB provides a cellular basis to encode conspecific sex independent of strain, but raises questions about whether the “pan-male” functional mitral cell type derives its activity from a similarly-tuned specialist receptor and about its apparent sexual dimorphism. More broadly, we consider the AOB’s role in conspecific recognition as a case study of how a sensory code is shaped by both biological purpose and engineering principle.

176 **Development- And Microbiome-Driven Bile Acid Signatures As Social Chemosignals In The Mouse Vomeronasal System**

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Early postnatal development is characterized by rapid maturation of the gut microbiome, which reshapes the host metabolic landscape and alters the excretion of bile acids (BAs). Fecal BAs are known to activate the accessory olfactory system (AOS), but the mechanisms by which these internal microbial and physiological cues are

transduced into external social chemosignals remain elusive. We performed mass spectrometric analysis of fecal samples from neonatal, conventional adult (CF), and germ-free (GF) mice. Taurine-conjugated BAs were significantly enriched in GF and neonatal samples compared to CF. UMAP dimensionality reduction and density-based cluster analysis showed that neonatal profiles were positioned closer to GF mice than to CF, suggesting that the neonatal metabolic landscape reflects an immature microbial state. Vomeronasal sensory neurons (VSNs) were then exposed to a panel of fecal extracts (neonate, juvenile, adult, and GF) and synthetic BAs, including cholic acid (CA), taurocholic acid (Tauro-CA), and tauro-β-muricholic acid (Tauro-β-MCA), and live volumetric Ca^{2+} imaging was performed using OCPI microscopy. Distinct VSN populations selective for neonate, juvenile and adult fecal samples were identified, demonstrating the AOS's ability to discriminate developmental stages. Specifically, the CA-responsive cluster overlapped neonate, juvenile, and adult responses, but not GF. Tauro-CA-responsive VSNs overlapped neonate, juvenile, and GF signatures, with minimal adult overlap. Similarly, Tauro-β-MCA-responsive neurons aligned with juvenile and GF, but showed little overlap with neonate or adult samples. These findings suggest that the AOS deciphers developmental and microbiome status via specific BA chemosignals, thereby linking internal physiological states to external communication.

178 **A Computational Framework For Multisensory Grounding Of Olfactory Representations**

Kordel France[1], Tian Yu[2], Michelle Niedziela[3]

[1]Scentience, Dallas, TX, United States, [2]Amai, Denver, CO, United States, [3]Nerdoscientist, Chalfont, PA, United States

Modern generative AI has made significant progress in modeling language and vision, yet still remains largely disconnected from the chemical properties of the physical world. Olfaction and gustation, though central to biological intelligence and environmental understanding, are typically absent from computational world models, leaving AI systems reliant on linguistic descriptions rather than chemical structure. We present a multimodal representational framework integrating olfactory signals at the molecular level with visual objects and linguistic descriptors within a shared joint-embedding space. Using publicly available datasets, molecular structures, images of physical objects, and odor-related language mapped into a unified multidimensional representation, we enables systematic exploration of relationships between chemical features, perceptual descriptors, and real-world contexts, supporting analyses of odor similarity, categorization, and cross-modal inference beyond chemistry alone. While we demonstrate that meaningful cross-modal alignment between chemical, visual, and semantic information is computationally feasible, results also reveal a key bottleneck: the scarcity of high-quality, curated chemosensory datasets that directly link chemical structure to human perceptual experience. By placing chemical senses on equal footing with vision and language, this framework offers a flexible platform for studying olfactory representation, multisensory integration, and semantic grounding. We invite discussion with the chemosensory community on how such models can be refined, validated, and expanded and how advances in chemosensory science can actively shape the next generation of multimodal AI systems.

10:15 - 12:15 PM	Bird Key
Industry Symposium: DATA DRIVEN TOOLS FOR SENSORY PREDICTION	

Chair(s): Kathryn Deibler, Xiaorong (Phoebe) Su, Ann-Marie Torregrossa, Casey Trimmer, Theresa White

10:15 **Introduction**

Predicting how chemicals give rise to human odor perception remains one of the most challenging problems in sensory science. While machine learning has begun to close the gap between molecular structure and perceptual experience, meaningful progress depends on integrating high-quality perceptual data, robust computational models, and biological insight. This work collectively addresses how olfaction can transition from a largely descriptive discipline to a predictive and mechanistically informed science.&#65533;A key focus is the generation of scalable, standardized odor quality data that can support modern modeling approaches. Efficient methods for capturing perceptual meaning at scale are essential to enable reliable structure: percept mappings and to ensure that predictions generalize across stimuli, concentrations, and contexts. Equally important is moving beyond isolated odorants to account for the complexity of real-world smells, including concentration effects and multi-component mixtures that define everyday olfactory experiences.&#65533;The integration of predictive models with receptor-level biology further strengthens the link between chemistry and perception, enabling not only improved prediction accuracy but also rational strategies for modifying odor experiences. Together, these efforts illustrate a convergent framework in which sensory methodology, artificial intelligence, and neurobiological understanding work in concert to advance digital representations of smell, support innovation in fragrance and odor control, and deepen fundamental insight into how humans perceive complex chemical environments.

10:25 **Predicting Odor Mixture Character From Chemical Structure**

Xuebo Song[1], Yuanfang Guan[2], Matej Hladiš[3,4], Nachman Keren[5,6], Maxence Lalis[3], Leonor Saiz[7], José Vilar[8,9], Evan Guerra[1,10], Yikun Han[10], Ashok Palaniappan[11], Maria Diaz[12], Gaia Andreoletti[12], Verena Chung[12], Robert Pellegrino[1], Pablo Meyer[13], Joel D. Mainland[1,14]

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The mapping between physical properties and perception is well-established in vision and audition, but remains poorly understood in olfaction. Recent advances in predictive modeling and availability of large-scale perceptual datasets have enabled reliable odor prediction from molecular structures. However, current models neglect concentration-dependent perceptual changes and focus on single molecules rather than real-world mixtures. To address these gaps, we organized the third DREAM Olfaction Challenge in 2025, focusing on two prediction tasks: (i) odor quality prediction for single molecules across concentrations, and (ii) prediction of the perceptual qualities of odor mixtures. We curated two complementary datasets: (i) 151 monomolecular odorants measured at two concentrations, and (ii) over 650 odor mixtures composed of 2, 3, 5, or 10 components, all profiled by trained panelists using a standardized 51-word odor lexicon. For single-molecule prediction, the top three teams achieved Pearson correlations ranging from 0.73-0.75, surpassing the measurement error on the provided data for the first task (r = 0.72). For mixtures, the top performing models achieved a Pearson correlation of 0.79, exceeding measurement error on the provided data for the second task (r = 0.73). These results significantly advance the mapping of chemical structure to human olfactory perception, establishing a foundation for digital representation of odor mixtures.

10:55 **Empirical Evaluation Of Human Odor Quality Datasets Supports The Use Of Lexical Methods For Collecting Big Data**

Emily J. Mayhew[1], Joel D. Mainland[2]

[1]Michigan State University, East Lansing, MI, United States, [2]Monell Chemical Senses Center, Philadelphia, PA, United States

Mapping stimulus chemistry to odor percept has long been an elusive goal, but recent strides in machine learning for olfaction suggest that the challenge is surmountable. Progress now requires large-scale perceptual datasets, yet existing olfactory data are limited to tens or hundreds of stimuli collected with unstandardized methods. Critically, the sensory method used to generate such data will profoundly affect data quality, collection efficiency, and model reliability—but no systematic comparison of methods exists. The field has historically made use of both lexical methods (using verbal descriptions) and non-lexical methods (i.e. similarity) to measure odor quality, although lexical methods are often critiqued as subjective and biased by verbal artifacts. In this study, we directly compared data resolution, test-retest reliability, and efficiency of data collection between 6 sensory methods (including lexical Rate-All-That-Apply, RATA, and non-lexical explicit Similarity, SIM) conducted by 2 sensory panels (highly or moderately trained) on a standardized set of 50 odor stimuli. We find that SIM generates the highest resolution (AUC=0.78) and test-retest reliability (R=0.96), followed by RATA (AUC=0.55, R=0.85), but that RATA is orders of magnitude more efficient (e.g. SIM is 29x slower with n=100 stimuli), especially as number of stimuli increases. Importantly, we also confirmed that odor spaces and distances generated by each method were highly correlated to each other, with odor distances extracted from RATA PCA closely approximating explicit SIM ratings (R=0.82). We conclude that rapid descriptive methods using a standardized lexicon (RATA) provide high quality data efficiently and recommend their use for the collection of odor quality "big data."

11:15 **Scaling Sensory Annotation Of Odor Mixtures With A Prior-Guided Sensory Annotation Tool**

Marissa L. Kamarck[1], Wesley Qian[1], Richard Gerkin[1,2]

[1]Osmo Labs, PBC, New York, NY, United States, [2]School of Life Sciences and School of Mathematical and Statistical Sciences, Arizona State University, Tempe, AZ, United States

Data-driven approaches to olfactory prediction require large volumes of high-quality, consistent sensory annotations—particularly for odor mixtures, which dominate real-world olfactory experiences but remain challenging to characterize at scale. At Osmo, we have built *Studio*, a caption-to-mixture platform for fragrance creation. A critical prerequisite for this effort is the ability to efficiently and reliably annotate complex odor mixtures within a shared, scalable taxonomy of olfactory terms. Traditional sensory annotation of mixtures is limited by low throughput, annotator variability, and cognitive load, especially when mixtures evoke overlapping or ambiguous perceptual qualities. To address these challenges, we developed a novel annotation tool designed to scale taxonomy-based mixture annotation while maintaining data quality and internal consistency. This tool introduces a structured annotation workflow supported by a probabilistic prior derived from a linear mixture model of odor components – using previous annotations or model predictions for each component – building on prior work in mixture perception and representation. This prior provides an initial hypothesis for mixture descriptors, which annotators can then refine based on perceptual experience. We describe the design of this new tool, the process by which priors are generated, and key tradeoffs of the approach including gains in annotation throughput and consistency, potential biases introduced by model-informed priors, and the extent to which human annotators can correct inaccurate priors. Together, these findings highlight a practical path toward collecting large-scale, high-quality mixture annotations to support the next generation of data-driven fragrance creation tools.

11:45 ***Predicting Sensory Outcomes: Integrating Receptor Neurobiology With Ai Tools***

Jessica H. Brann, Daniel A. Raps, Georgia M. Pierce, Michael Cohanpour, Gary Marr, Giulia Papiani, Lily Wu, Randy Arroyave, Bénédicte Le Calve, Francesco Moriello, Ben Smith, Casey Trimmer, Patrick Pfister
dsm-firmenich, New York, NY, United States

Malodors such as moldy, earthy notes on fabrics present a persistent consumer challenge, and are often linked to the earthy compound geosmin. To address this, we developed an odorant receptor-based strategy targeting odorant receptors implicated in earthy perception. Bayesian predictive and random forest modeling were applied to predict receptor tonalities, enabling prioritization of several OR targets. OR11A1 emerged as a key contributor, supported by *in vitro* expression studies and prior findings associating OR11A1 activity with intensity and pleasantness ratings for the earthy compound 2-ethyl fenchol. We next screened a large set of compounds for their ability to modulate OR11A1 activity in the presence of geosmin, identifying several candidates for sensory evaluation. Building on these insights, selective inhibition of OR11A1 in the presence of geosmin significantly reduces perceived earthy intensity, validating receptor-level modulation as an effective approach. Understanding of OR11A1 activity and modulation was thus integrated into market fragrances designed to reduce moldy malodor perception, yielding positive results when evaluated in consumer tests. These findings highlight the impact of integrating computational modeling with receptor-targeted interventions to deliver meaningful and rational odor control solutions for everyday consumers.

10:15 - 12:15 PM	Sawyer Key

THE APPETITION AXIS: INTEGRATING PHASIC SENSORY AND PHYSIOLOGICAL SIGNALS TO DRIVE INGESTION

Chair(s): Lindsey Schier

10:15 **Introduction To The Appetition Axis: Integrating Sensory Cues To Drive Ingestion**

Lindsey A. Schier
Department of Biological Sciences, University of Southern California, Los Angeles, CA, United States

Meal size is largely determined by sensory information arising from the oral cavity and proximal gut during active ingestion. While oral and post-oral signals have mainly been studied in the context of their opposing effects on meal size, with flavor driving intake of nutritious substances and gut feedback terminating intake, Tony Sclafani and others have importantly demonstrated that nutrients can rapidly stimulate intake from post-oral sites of action, increasing meal size in the short term, and reinforcing appetitive and consummatory responses to associated oral cues over the long term through learning, phenomena collectively termed appetition (as opposed to satiation). This symposium will expand the original concept of appetition by exploring: the sequence of post-oral signals that arise during digestion and their differential effects on food learning (Myers), how metabolic cues shape taste perception and reward (Chometton), how non-caloric, essential nutrients such as water, engage appetition-like mechanisms (Daniels), and provide new evidence for the role of hypothalamic melanin-concentrating hormone in the mediation of nutrient-driven appetition (Kanoski). Together, these talks position appetition as a distributed and plastic process and suggest new directions for dissecting how chemosensory, physiological, and central signals converge to control ingestion.

10:25 **Phasic Gut Feedback Shapes Flavor-Nutrient Learning**

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

It has been a longstanding view that macronutrient molecules (especially sugars and fats) have palatable orosensory properties that stimulate food intake, but that their post-oral effects are generally inhibitory, triggering negative feedback signals that cause meal termination. However, a body of evidence has recently emerged establishing that nutrients sensed in the gut can give rise to immediate *positive* feedback signals (termed 'appetition,' in contrast to the better-understood 'satiation' signals) that stimulate ongoing intake, increase meal size, and produce learned preferences for tastes and flavors in the meal. This presentation will provide an overview of the behavioral properties of appetition, including evidence from our work in a rat model that within the first several minutes of a meal, animals psychologically 'attribute' gut nutrient sensing to the specific flavor of the food they are currently consuming. Although appetition acts to increase intake and steer preference towards nutrient-dense foods, the relationship between appetition, flavor-nutrient learning, and diet-induced obesity is complex. We have found that with long-term access to high-fat/sugar diet, rats who gain the most weight also show the strongest appetition responses, including both immediate intake stimulation by gut nutrient infusion and learned preference for nutrient-paired flavors. However, rats selectively bred to be highly prone or resistant to diet-induced obesity show no differences in appetition responses prior to obesogenic diet access, suggesting that sensitized appetition is a consequence, not a cause, of chronic overeating and/or obesity. The presentation will conclude with an overview of some important unanswered questions about the psychology and neurobiology of appetition.

10:55 **Nutritional Reprogramming Of Oral Glucosensing**

Sandrine Chometton[1], Lindsey A. Schier[2]
[1]Université Bourgogne Europe, Institut Agro, CNRS, INRAE, UMR CSGA, Dijon, France, [2]Department of Biological Sciences, University of Southern California, Los Angeles, CA, United States

Glucose is an essential source of energy for all living organisms. Because this nutrient is mainly provided by the diet, it is necessary for the body to rapidly detect and motivate the ingestion of glucose-containing substances. The oral taste system is critical for recognizing nutrients in the environment and initiating ingestion. Chemically- and metabolically-diverse compounds including simple sugars, like glucose, low-calorie sweeteners, and D-amino acids engage a common "sweet taste" receptor (T1R2+T1R3), yet rodents will preferentially consume glucose over these other substrates over the long term. Our recent work demonstrates that experience with the post-ingestive effects of two metabolically distinct sugars, glucose and fructose, enables animals to subsequently discriminate these two initially similar-tasting compounds based on orosensory information, and generates a preference for glucose over fructose. This result has also been observed in mice lacking the canonical sweet taste receptor, showing that a T1R-independent pathway is involved. In this talk, I will present recent evidence we uncovered for how the post-ingestive effects of sugar reprogram metabolism-dependent and -independent glucosensing pathways in the taste bud cells, and amplify the responsiveness of taste neurons in the rostral nucleus of the solitary tract to oral glucose, in a T1R-independent fashion. Overall, these findings expand our understanding of orosensory mechanisms underlying glucose appetition.

11:15 **Fluid Balance Revisited: Oral, Postoral, And Central Signals Driving Water Intake**

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

Discussions of appetition have largely focused on food intake, although a significant amount of research on the topic has provided 'food' in fluid form. Although presenting 'food' in liquid form is common and often necessary, the large amount of water consumed as the vehicle for the food creates a potential confounding variable. For this and other reasons, it is important to ask if the concept of appetition can be extended to include thirst and water intake. ‘Appetition,’ however, is used inconsistently as a term, making it challenging to determine if its application to fluid intake is ever appropriate. On one hand, the term is used to refer to feedback from the gut that acts to increase the size of a meal. In this sense, the focus on the gut likely makes the term inapplicable to water consumption. If, on the other hand, the specificity of the gut is less important to the overall concept, and appetition also encompasses signals from the oral cavity that promote intake, then findings from our laboratory and from others showing sensitized responses to dipsogens fit into the appetition framework. In this sense, water intake sensitization also could serve as a new model of appetition, with a yet to be discovered neural or hormonal signals mediating the response. A discussion of these issues, as well as a description of the findings related to sensitization of water intake, will be presented.

11:45 **Mch And The Drive To Continue: Hypothalamic Control Of Nutrient-Based Appetition**

Scott E Kanoski
Department of Biological Sciences, University of Southern California, Los Angeles, CA, United States

Peripheral nutrient detection is rapidly communicated to the brain and translated into decisions about meal size and food choice. While the neural mechanisms that limit intake and terminate meals are well characterized, the central processes that amplify ingestion in response to nutrient signals – i.e., “appetition” – remain poorly understood. The hypothalamus, as a central hub for the integration of nutrient sensing and motivated behavior, represents a likely target for the central mediation of appetition. This presentation will review data establishing a role for the hypothalamic neuropeptide melanin-concentrating hormone (MCH) as a key central mediator driving nutrient-based appetition. Based on emerging findings, a framework will be presented whereby different populations of MCH neurons located in the lateral hypothalamus and the zona incerta promote distinct components of appetition.

12:15 - 2:00 PM	Lunch On Own
Lunch On Own	

12:15 - 2:15 PM	Pavilion Lawn
Trainee Lunch Activity	

Giant Jenga, Cornhole and Ladderball will be available on the Pavilion Lawn
Paddle boats by Pirate Island

12:30 - 1:30 PM	Offsite
Outreach Event: President Barack Obama Library	

2:00 - 3:30 PM	Bird Key
The Barry Davis NIH Funding Workshop	

2:00 **Nih Updates For Early And Established Investigators**

2:30 **Nidcd Workshop For Trainees And New Investigators**

2:00 - 3:30 PM	Jacaranda Hall
Practical demonstrations of clinical chemosensory tests	

This practical session is meant to provide a very practical overview about techniques that are used in a clinical context to assess chemosensory functions, including olfactory, gustatory, and trigeminal functions. In addition, techniques to address psychological/cognitive issues related to olfactory function and dysfunction will be shown. The various techniques will be presented by researchers experienced in clinical chemosensory research, including Bob Pellegrino from Philadelphia, Caroline Huart from Brussels, and Akshita Joshi from Bethesda and Thomas Hummel from Dresden.

There will be 4 stations, and the participants would rotate clockwise through stations 1 to 4. They will stay at each station for 15 min. The 4 stations will be: Station 1: Smell testing (e.g., Sniffin Sticks, UPSIT, CCCRC test, SSParoT, retronasal testing): Akshita Joshi, Bethesda, MD, USA; Station 2: Taste testing (e.g., taste sprays, taste strips, electrogustometry, PROP/PTC test): Robert Pellegrino, Philadelphia, PA, USA; Station 3: Trigeminal testing (e.g., lateralization, AMMOLA-test, oral capsaicin test, CO2 threshold): Anna Kristina Hernandez, Dresden, Germany; Station 4: Psychological testing/questionnaires (e.g., SNOT, QOD, WHO wellbeing, MOCA): Jonathan Overdevest, New York, NY, USA

Chair(s): Thomas Hummel

3:30 - 5:30 PM	Pavilion
Poster Session II	

101 **Don Tucker Finalist: Olfactory Coding Across Ventral Subregions Of The Hippocampus**

Anna C. Kolstad[1,2], Karol P. Szymula[1,2], Krishnan Padmanabhan[1,3,4]

[1]Department of Biomedical Engineering, University of Rochester, Rochester, NY, United States, [2]Medical Scientist Training Program, University of Rochester School of Medicine and Dentistry, Rochester, NY, United States, [3]Department of Neuroscience, University of Rochester School of Medicine and Dentistry, Rochester, NY, United States, [4]Center for Visual Science, University of Rochester, Rochester, NY, United States

While ventral hippocampus (VH) historically has been associated with memory, navigation, and anxiety, evidence increasingly suggests that chemosensory stimuli may influence VH neural responses. Although olfaction is involved in many hippocampal-related behaviors, how VH represents olfactory stimuli remains an open question. As the ventral CA1 (vCA1) subregion of VH receives both direct projections from olfactory cortex and indirect projections via the lateral entorhinal cortex through the CA3 and dentate gyrus (DG) VH subregions, vCA1 is likely a hub for both chemosensory and cognitive encoding. A necessary first step toward understanding how VH integrates sensory and cognitive representations is to identify what features of olfactory stimuli such as odorant identity are encoded for in neural firing, and how these patterns of firing vary across VH

subregions. To address this question, we performed high-density extracellular electrophysiology recordings across vCA1, CA3, and DG in awake head-fixed 2-4-month-old C57BL/6J mice as they ran on a wheel while passively exposed to a panel of eleven odorants. When we examined neural activity from eight mice (4F/4M; n = 79 vCA1 units, n = 59 CA3 units, n = 28 DG units), we found across all three subregions neurons that are tuned to odors. Both increased and decreased single unit firing in response to odors was observed in all three subregions. Odor-tuned neurons were more prevalent in vCA1 compared to CA3 (67% vs. 34%, P <0.001). Odorant tuning profiles were more similar across DG neurons compared to in vCA1 or CA3. Taken together, our work suggests that different VH subregions have distinct strategies for encoding odors, suggesting that chemosensory stimuli may differentially impact cognitive representations across VH.

103 **Achems Undergrad Finalist: Inhibition Of Focal Adhesion Kinase Limits Axon Growth From Olfactory Sensory Neurons Following Injury**

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

Regeneration of olfactory sensory neurons (OSNs) in the adult olfactory epithelium (OE) maintains the sense of smell. New OSNs extend their axons from the OE to the olfactory bulb via the lamina propria. Adhesion inhibition restricts axon growth by blocking cell-substrate interaction, including integrin and extracellular matrix molecules. Integrin signals through FAK. To determine whether FAK affects axon growth, we fate-traced Tdtomato (Tdt)+ axons in the lamina propria in Mash1$^{Cre\text{-}Tdtomato\ (Tdt)}$ mice in which Tdt protein was expressed in Mash1+ neuronal progenitor cells. We measured GAP43+ axons that came from newly generated immature OSNs following injury and extended into the lamina propria. Mash1$^{Cre\text{-}Tdt}$ mice were treated with methimazole to deplete OSNs and initiate neuroregeneration. At 3-5 days, we treated mice with saline or FAK inhibitor, FAK14, intranasally. 24 h later, GAP43+ axons extended into the lamina propria. Compared to saline, FAK14 reduced GAP43+ area, suggesting that FAK14 limits axon growth and extension. FAK14 also appeared to reduce Tdt+ axons in the lamina propria. Olfactory ensheathing cells (OECs) facilitate axon growth. To examine whether OECs contribute to the effect of FAK inhibition, we selectively knocked out FAK in OECs of GFAP^{Cre}-FAK$^{fl/fl}$ mice and performed bulbectomy to deplete OSNs. At 5 days post-bulbectomy, GFAP^{Cre}-FAK$^{fl/fl}$ mice had less GAP43+ area in the lamina propria than FAK$^{fl/fl}$ controls. Together, these data suggest that FAK promotes axon growth and extension, possibly through OECs. Thus, activation of FAK signaling may facilitate recovery of the sense of smell following injury, virial infection or aging.

105 **Don Tucker Finalist: Distinguishing The Olfactory Epithelium Using An Fda-Approved Dye & Machine Learning Methods**

Skylar A Suarez[1], Emily A Gibson[1], Diego Restrepo[2, 3]
[1]Department of Bioengineering, University of Colorado Anschutz Medical Campus, Denver, CO, United States,
[2]Department of Physiology & Biophysics, Stony Brook University, Stony Brook, NY, United States,
[3]Department of Cell & Developmental Biology, University of Colorado Anschutz Medical Campus, Denver, CO, United States

The olfactory epithelium (OE) is a specialized tissue located deep within the nasal cavity that contains stem cells (globose basal cells and horizontal basal cells), supporting cells and olfactory sensory neurons (OSNs) that are responsible for detecting odorants and transmitting olfactory information to the brain. Anosmia is common in aging and can be a symptom of respiratory infections, medication side effects, and some neurological disorders. As humans age, some OE areas undergo neurogenic exhaustion as their OSNs stop being replaced by globose basal cells, leading to patchiness. In other conditions, the OE may be damaged. As a result, the OE exists in patches surrounded by exhausted OE and respiratory epithelia (RE) within the nasal cavity. These patches vary in size and the OSNs are not uniformly distributed throughout, especially in aging and conditions related to olfactory dysfunction. Therefore, the ability to visualize the OE in vivo can assist with assessment of the cause of aging-related anosmia and olfactory dysfunction. It can also assist in observing and quantifying any changes in OE associated with progression or treatments. This project explores using Indocyanine Green to visualize nasal epithelia tissue structure, followed machine learning and deep learning methods to distinguish the OE from its surrounding respiratory epithelia. Using texture analysis, the machine learning methods reached ~80% classification accuracy, while direct deep learning methods reached ~90% accurate classification of OE images.

107 **Achems Undergrad Finalist: Spatial Gene Expression Profiling Reveals Acute And Persistent Olfactory Bulb Neuroimmune Responses To Sars-Cov-2 Infection**

Yaejin Kim[1], Jiaying Liu[1], Anthony Weidner[1], Garret Roth[1], Lark Coffey[2], Hongwei Liu[2], Qizhi Gong[1]
[1]Department of Cell Biology and Human Anatomy, UC Davis School of Medicine, Davis , CA, United States,
[2]Department of Pathology, Microbiology & Immunology, UC Davis School of Veterinary Medicine, Davis, CA, United States

Olfactory loss is a common clinical symptom of COVID-19, caused by SARS-CoV-2 infection. The olfactory mucosa is constantly exposed to the external environment and has direct access to the olfactory bulb (OB) of the brain. This unique anatomical arrangement may facilitate neuroimmune interactions that could contribute to neuropathogenesis in the central nervous system. Although the olfactory mucosal response to SARS-CoV-2 infection has been characterized, it remains unclear whether this mediates inflammatory responses within the OB and whether these result in long-term neuropathological changes. To address these questions, we performed

spatial gene expression analysis to characterize acute (2 days post-infection [DPI]) and long-term (3 months post-infection [MPI]) changes in the mouse OB following SARS-CoV-2 infection. Xenium datasets were generated using the mouse Brain gene panel with an additional 99 custom gene targets. OB sections from mock- and SARS-CoV-2-infected wild-type and 5xFAD animals were analyzed and compared, with a total of 55,612 cells analyzed. At 2 DPI, we observed significant upregulation of antiviral gene expression in the olfactory nerve layer and the glomerular layer of the infected OB, while these signals were comparable to controls at 3 MPI. Consistent with olfactory mucosa dysfunction during acute infection, immediate early genes, *Fos* and *Arc*, in the glomerular and granule cell layers of the OB were significantly decreased at 2DPI. SARS-CoV-2 infection also resulted in differential expression of neuroplasticity genes (Cpne6, Calb2) in 5xFAD compared to wild-type mice at 3MPI. Our spatial gene expression data indicate that the inflammatory signals enter the OB via the olfactory pathway and may contribute to long-term neurodegeneration in the OB.

109 **Achems Undergrad Finalist: Identification Of An Olfactory Receptor Involved In Newborn Rabbits' Responsiveness To The Mammary Pheromone: Molecular Genetic Evidence**

Victoria Ko[1], Gérard Coureaud[2], Patricia Duchamp-Viret[2], Hiroaki Matsunami[1]

[1]Department of Molecular Genetics and Microbiology, Duke University School of Medicine, Durham, Durham, NC, United States, [2]Lyon Neuroscience Research Center - ENES team, CNRS/Inserm/Lyon 1 and Jean Monnet Universities, Lyon, France

Successful mammalian development depends on a newborn's ability to locate the mother's milk and initiate sucking. In European rabbits (*O. cuniculus*), this behavior is driven by olfactory cues through the detection of a pheromone present in the mother's milk. Exposure to mammary pheromone (MP, 2-methylbut-2-enal) elicits typical head searching - oral grasping behavior in rabbit pups (Schaal, Coureaud et al. 2003). Through pS6 IP-Seq together with heterologous cell assays, we identified olfactory receptor 2D2-like as responsive to MP (EC50 $10^{-4.5}$ M), which we designate as a mammary pheromone receptor (MPR). However, whether MPR mediates newborn behavior remains unclear. We aimed to identify an antagonist for MPR to investigate whether receptor inhibition also inhibits newborn behavior. We used a heterologous cell system to express the olfactory receptor and stimulated with each chemical. Olfactory receptor activities were measured with Glosensor cAMP assays. Through screening a panel of 366 odorants, we identified two compounds, damascenone (Da) and β-ionone (β) (Da IC50 9.75×10^{-5} M, β IC50 2.72×10^{-5} M), as both potent and effective antagonists to MPR in the presence of MP. The antagonistic effect was observed to be dose-dependent for both β and Da. To determine the selectivity, MPR was also stimulated with ethyl isobutyrate (EI). EI had no effect on MPR activity alone and did not inhibit the receptor in the presence of MP. *In vivo*, exposure to Da or β, but not EI, suppressed pups' sucking-related responses to MP at moderate concentrations (Coureaud et al., this conference). Together, these findings indicate that MPR is a key mediator of MP processing and behavioral responsiveness to MP in newborn rabbits, and provide new insight into the molecular basis of early olfactory-driven behavior.

111 **Achems Undergrad Finalist: Testing A Relationship Between Odor Mixture Perception And Working Memory Capacity**

Elijah Wakefield[1], Chong Zhao[2,3], Leslie M. Kay[1,2,3]

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Previous research shows that humans cannot reliably identify more than three or four odorants in multicomponent mixtures. It is claimed that this upper limit reflects an inherent limitation in olfactory perception. An alternative explanation incorporates working memory capacity. Recall of odorants' learned names, which constitutes "identification," places demands on verbal working memory in addition to odor knowledge. Therefore, the presumed olfactory identification limit may be influenced by working memory capacity, as examination of a complex mixture occurs over the space of a few sniffs, mirroring working memory time spans. In the present study we explore the possibility that working memory capacity may be partly responsible for the observed odor component identification limit. We replicate previous research with a new set of odorants–a set of "good blenders" whose mixtures yield a homogenous percept, making identification of individual odorants presumably more difficult. We add a visual working memory test to test the hypothesis that mixture component identification is correlated with working memory capacity. The first wave of data collection indicates a possible correlation between working memory capacity and component identification in complex mixtures, encouraging support for our hypothesis. Participants are unable to reliably identify beyond three or four odorants in a mixture, and odor identification performance scales positively with visual working memory scores ($r = 0.68$, but non-significant with 5 subjects). The second wave of data collection is underway (10 additional subjects; planned total is 40 subjects).

113 **Achems Undergrad Finalist: Optimizing Surgical Access To The Nodose Petrosal Ganglia**

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The sense of taste provides more information to our body than the mere identification of the food we eat. In mammals, taste serves as an indicator of pleasure, a mechanism of survival, and a way to evaluate the nutritional content of food. Taste begins at the tongue, where taste buds, each containing taste receptor cells (TRCs) can be found. Taste buds are distributed within three papillae:The circumvallate and foliate papillae are found at the posterior portion of the tongue, housing TRCs innervated by nerve fibers originating from the petrosal nodose jugular (PNJ) ganglia;fungiform papillae are found at the anterior portion of the tongue and receive projections from the geniculate ganglia. However, it is still unknown how the taste ganglion neurons connect to the taste

cells on the tongue. To address this, we optimized surgical access to the PNJ ganglion to enable direct labeling and manipulation of the first order taste neurons. Here, as proof of principle, we will present results from direct delivery and infection of AAV viral vectors in the PNJ showing selective labeling of these neurons and their projections with tdTomato red fluorescent protein. Thus, understanding how information is relayed by the peripheral taste system is the first step in uncovering the mechanisms that drive behavioral responses to taste.

115 **Don Tucker Finalist: The Role Of Stimulus Temperature On Salt Taste Perception In Mice.**

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Stimulus temperature influences taste perception and consumption patterns, yet its effects remain poorly understood. This is critical for table salt (NaCl) as temperature-driven consumption changes can increase hypertension risk. We examined how stimulus temperature affects motivational and sensory-discriminative properties of NaCl and non-sodium salt (KCl). Water-deprived mice strongly preferred cool (14˚C) over warm (36˚C) stimuli in brief-access tests regardless of salt identity, concentration, or water alone. Progressive ratio testing confirmed cool stimuli possess greater appetitive efficacy independent of salt content, indicating brief-access procedures poorly assess stimulus temperature effects under water deprivation conditions. In contrast, operant tasks revealed robust stimulus temperature effects on sensory-discriminative function. In detection tasks where mice identified each salt from water, sensitivity to both salts was enhanced at 36˚C versus 14˚C, with lower detection thresholds at warm stimulus temperatures. Critically, when mice distinguished NaCl from KCl with intensity controlled by anchoring concentrations at detection thresholds, discrimination performance was significantly impaired at 36˚C versus 14˚C, indicating the two salts become perceptually more similar at warmer stimulus temperatures. Stimulus temperature profoundly modulates sensory-discriminative properties: warm stimuli enhance detection sensitivity while reducing qualitative discriminability between sodium and non-sodium salts. This temperature-induced perceptual similarity suggests KCl may serve as a more effective NaCl substitute in warm foods, with important implications for sodium reduction strategies.

117 **Don Tucker Finalist: Investigating Establishment Of Sox9+ Taste Progenitors In The Circumvallate Papilla**

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Gustation is mediated by taste buds housed in specialized papillae on the tongue. The murine circumvallate papilla (CVP) at the posterior lingual midline contains hundreds of taste buds and forms a continuous epithelium with von Ebner's minor salivary glands (VEG). Each bud contains short-lived taste bud cells (TBCs) that detect taste stimuli and are continuously renewed by progenitors outside buds. We have identified SOX9+ cells in the CVP/VEG junctional epithelium as a novel, long-term taste progenitor population in adult mice; however, when and how this population is established remains unexplored. CVP development begins at embryonic day (E)12.5 with formation of a *Shh*+ placode. Via HCR, we find limited *Sox9* expression in the *Shh*+ placode. However, by E14.5 *Sox9* is distinct from dorsal *Shh*+ expression and robustly expressed in ventral invaginating trenches. Lineage trace of embryonic SOX9+ cells initiated at E14.5 reveals SOX9+ cells contribute to junctional epithelium but not to initial taste buds at E17.5. Conversely, *Shh*+ cells lineage-labeled at E14.5 generate initial taste buds but not junctional epithelium. We are now assessing if embryonic Sox9+ cells function as taste stem cells postnatally. Further, we are testing the functional role of Shh signaling in development of SOX9+ cells and junction formation as *Ptch1* and *Sox9* expression overlap during trench invagination. Preliminarily, conditional genetic deletion of Shh signaling prior to CVP trench formation blocks CVP morphogenesis and junction formation. Our early findings suggest a model where Shh signaling is necessary for adult SOX9+ taste progenitor establishment in the CVP junctional epithelium. Support: T32GM141742, F31DC023482 to AS, and R01 DC021865 and DC018489 to LAB

119 **Achems Undergrad Finalist: Palatability-Dependent Activation Of Orexin Neurons In The Lateral Hypothalamus**

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Orexin neurons are a distinct population in the lateral hypothalamus (LH) well characterized for their role in feeding and arousal, especially regarding palatable, high-calorie food. Prior work has demonstrated single-unit LH taste responses promptly reflect palatability; however, orexin neurons' role in processing the hedonic value of taste is yet to be characterized, as the majority of work in orexin only includes high-value or hedonically positive stimuli. The present research examines cFos reactivity in orexin neurons in rats given intraoral taste solutions that span the palatability spectrum (either 0.3M sucrose, 5mM quinine, or water). Preliminary results indicate that sucrose-receiving animals show a higher percentage of cFos-positive orexin neurons than those receiving water or quinine, suggesting orexin neurons preferentially respond to palatable taste stimuli. To elucidate the role of palatability in driving this response, independent of caloric or post-ingestive feedback, a second experiment was conducted with sucrose made aversive via conditioned taste aversion (CTA), following pairing with 0.3M LiCl. If orexin neurons are palatability-responsive, we hypothesize that the CTA animals' orexin response to

sucrose will be significantly lower than in saline control as a result of the tastes' inversion in palatability. These findings will directly implicate orexin neurons' taste response as palatability-dependent units in the LH.

121 **Achems Undergrad Finalist: Sex-Dependent Estrogenic Regulation Of Peripheral Fat Taste Signaling**

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Recent work demonstrates sex differences in dietary fat perception and preference, yet the cellular mechanisms underlying these differences remain poorly understood. Estrogen influences feeding behavior, but its role in peripheral fat taste signaling remains incomplete. Expression studies indicate that estrogen receptors, including estrogen receptor alpha (ERα) and the G protein–coupled estrogen receptor 1 (GPER1), are present in taste receptor cells (TRCs) and may modulate fatty acid–evoked signaling pathways. To investigate estrogen's contribution to fatty acid taste transduction, we employed a multidisciplinary approach that combined ovariectomy, ratiometric calcium imaging, and pharmacological interventions in genetically identifiable taste cell populations. Intracellular calcium responses to long-chain polyunsaturated fatty acids were examined in isolated taste cells from male mice and from intact and ovariectomized female mice. Transgenic mouse lines expressing GFP-PLCβ2 and GFP-GAD67 were used to distinguish Type II and Type III TRCs, respectively, enabling cell–type–specific analysis of estrogenic modulation. We hypothesized that estrogen deprivation alters fatty acid–evoked calcium signaling in TRCs, primarily through effects on Type II cells. Our results indicate that estrogen significantly modulates fatty acid–evoked responses in Type II TRCs via the TRPM4/TRPM5 signaling pathway. Additionally, loss of estrogen following ovariectomy disrupts the function of key fatty acid signaling components, including calcium-release activated calcium channels and CD36, in a sex-dependent and cell–type–specific manner. Together, these findings elucidate how estrogen shapes peripheral fat taste signaling and provide mechanistic insight into sex-specific differences in dietary fat perception and intake.

123 **Don Tucker Finalist: Miraculin (Miracle Berry) As A Potential Mitigation To Improve Taste Perception In Head & Neck Cancer Patients**

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Head & neck cancer patients frequently experience taste alterations due to treatment. Oral zinc & baking soda rinses are insufficient. This study aimed to evaluate whether miracle berry (MB) may serve as an effective intervention for taste dysfunction. We conducted a preliminary, prospective, self-controlled study including 19 patients diagnosed with HNC who had undergone radiation (avg. 3647 Gy), surgery, and/or chemotherapy (avg. 4.94). Participants completed the MD Anderson Head and Neck Symptom Inventory (MDASI-HN) and the extended NIH Toolbox Taste Test assessing sweet, salty, sour, bitter, and spicy solutions. Confidence, intensity, and pleasantness were rated.14/19 patients self-reported loss; however, objective identification differed only for bitter taste, which was correctly identified by 5/14 patients with self-reported loss, compared to 4/5 patients without loss. Following intake, patients correctly identified sweet solutions (15 vs. 17), with reduced identification accuracy for other tastes. Overall identification scores did not significantly change (3.06 2.8, $p=0.72$). MB intake was associated with decreased intensity of sweet (60 vs 38.1, $p<0.05$) & spicy (72.6 vs 47.5, $p<0.05$), and increased intensity of bitter (31.5 vs 57.2, $p<0.05$). Sweet pleasantness significantly decreased post-MB (78.2 vs 48.75, $p<0.05$). Confidence identifying bitter increased following MB (40.8 vs 62.2), while confidence identifying spicy decreased (80 vs 52.5, $p<0.05$). Baseline taste intensity correlated with lack of appetite ($r=-0.50$, $p<0.05$). Dry mouth significantly correlated with baseline & MB intensity; & MB taste identification ($r=-0.42, -0.51, -0.48$; $p<0.05$). This shows that while MB produces shifts in taste identification, changes in subjective measures are complex and variable.

125 **Don Tucker Finalist: Sweetness Preference And Eating Behaviors In Habitual And Non-Habitual Consumers Of Low-Calorie Sweetened Products.**

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Low-calorie sweeteners (LCS) are commonly consumed as alternatives to sugar; however, their long-term influence on sweet taste perception and eating behaviors remains unclear. This cross-sectional study investigated whether regular LCS intake is related to sweetness preference, consumption of sugar-sweetened beverages (SSBs), food cravings, and eating behavior patterns. Healthy adults between 18 and 64 years of age were classified as habitual LCS consumers (≥5 LCS-containing products per week; $n = 44$) or non-habitual consumers (<1 LCS-containing product per week; $n = 45$). Sweetness preferences across varying concentrations of sucrose and sucralose were evaluated using the Monell two-series forced-choice paired-comparison procedure. Food cravings, eating behaviors, and beverage intake were assessed using validated instruments, including the Food Craving Inventory, Dutch Eating Behavior Questionnaire, and Beverage Intake Questionnaire. No significant group differences were observed in preferred sweetness levels for sucrose ($p = 0.9$) or sucralose ($p = 0.7$), frequency of food cravings ($p = 0.7$), or daily SSB consumption ($p = 0.3$). In contrast, habitual LCS consumers reported higher levels of emotional, external, and restrained eating ($p = 0.04$), an association that persisted after adjusting for body weight. Collectively, these results indicate that habitual LCS consumption neither replaces

SSB intake nor alters sweetness preference. Rather, higher LCS use may reflect a broader pattern of preference for sweet-tasting foods and eating behaviors linked to overeating.

127 **Don Tucker Finalist: Tex15 Controls Runaway Olfactory Receptor Transcription To Necessitate Diverse Olfactory Receptor Choice**

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Hundreds of different types of odorant receptors (ORs) are expressed by olfactory sensory neurons (OSNs) in the mouse olfactory epithelium (MOE), but each OSN expresses only one allele of one of OR gene. The choice of a single OR gene occurs as neuronal progenitors differentiate and is accompanied by widespread changes at OR gene loci. How these processes interact to effectuate diverse but singular OR across all OSNs remains poorly understood. We show that Testes expressed gene 15 (Tex15) is transiently expressed by OSN progenitors and that it is required for generating a diverse population of OSNs subtypes. Mice bearing a Tex15 null allele have reduced H3K9me3 deposition over OR clusters. This is accompanied by a dramatic reduction in OSN diversity, with OR choice dramatically skewed towards OR genes that are normally expressed at the early stages of differentiation and then repressed. Tex15 KO mice fail to repress these ORs and generally exhibit increased levels of OR transcription in OSN progenitors. These early expressed OR genes preferentially assemble into the Greek Island enhancer hubs that control OR gene choice. This breakdown of the normal choice process is accompanied by a disruption of the spatial patterning of OR gene expression, where upregulated OR genes predominate in the ventral MOE. These findings reveal a novel mechanism that represses the expression of the earliest expressed OR genes, allowing OR choice to sample the full repertoire of OR genes. In the absence of this mechanism early transcription of OR genes result in a deterministic pattern of OR gene selection leading to a few ORs getting highly expressed. Taken together these results establish that the regulation of OR transcription in progenitor cells is central to the mechanism that leads to diverse but singular OR choice.

129 **Identification Of An Olfactory Receptor Involved In Newborn Rabbits' Responsiveness To The Mammary Pheromone: Behavioral EvidencE**

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European newborn rabbits (*Oryctolagus cuniculus*) rely on olfaction to find and grasp their mother's nipples during her brief daily visit to the nest for nursing. In particular, they are predisposed to respond to the mammary pheromone (MP; 2-methylbut-2-enal), which is emitted in milk by lactating females and triggers the orocephalic movements typical of pups' nipple-search behavior. MP is processed by the main olfactory system, where it strongly activates olfactory sensory neurons. Until now, the molecular receptor(s) involved in its peripheral processing had remained unknown. Here, we first used molecular profiling and identified a MP (2D2-like) receptor candidate, MPR. We then screened potent odorant antagonists *in vitro* (Ko et al., this conference). Second, we tested pups' behavioral responsiveness to MP mixed with MPR antagonist - β-ionone (β) or damascenone (Da) - or with a non-antagonist control, ethyl isobutyrate (EI). MP was used at an optimal concentration for behavioral effects (10^{-6} g/ml) and mixed with the other odorants at various concentrations (10^{-2} to 10^{-12} g/ml). At very high concentrations, all three odorants reduced responsiveness to MP, likely due to non-specific masking, whereas at the lowest concentrations, none impaired responses. A key finding was the disappearance of responsiveness to MP+β or MP+Da at an intermediate concentration corresponding to the MP/antagonist ratio of 1.5, indicating that antagonistic mechanisms at the level of MPRs result in a loss of MP perception (EI had no effect at this ratio). Combined with the findings of Ko et al., these results demonstrate that MPR plays a key role in the peripheral processing and detection of MP in newborn rabbits, thereby facilitating the behavioral response that guides them towards the nipples for sucking.

131 **Genome-Wide Association Study Meta-Analysis Of Dietary Intake In Two Cohorts Identifies Seven Novel Olfactory Receptor Associations**

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Genome-wide association studies (GWAS) of food liking and intake have identified hundreds of genetic associations, including loci near several olfactory and taste receptor genes. These represent an important first step in understanding how smell and taste perception shape preferences, behavior, and health. To identify more novel associations between dietary intake and taste and olfactory receptor loci, we performed GWAS meta-analysis of 38 self-reported dietary intake traits (e.g., beef, bread, cheese, coffee, tea, vegetables, fruit, fish, and alcohol) in ~450K individuals in UK Biobank and ~23K females in Women's Genome Health Study. GWAS were conducted in European ancestry and adjusted for age, sex (UK Biobank only), center/location, and ancestry via principal components. Association results were interrogated across 788 olfactory receptor genes, including pseudogenes, downloaded from The Human Olfactory Data Explorer and a manually curated set of 36 taste-related genes (including 27 taste receptors). Novel loci were defined as genome-wide significant ($P<5x10^{-8}$) and

independent (R^2<0.10) from loci reported in the previous UK Biobank–only diet GWAS. We identified seven novel olfactory receptor loci associated with diet. Three loci, nearest *OR52K1, OR52N4, OR1F1*, were associated with raw and cooked vegetable intake. While *OR1F1* odorants overlap plant-derived volatiles, little is known about the functional roles of *OR52K1* and *OR52N4*. Additional associations were observed for beef intake (near *OR6B3* and *OR2V2*), fish intake (near *OR7E160P*), and fruit intake (*OR4S1*). These findings extend prior diet GWAS associations to include novel olfactory receptor loci, highlighting promising targets for downstream functional characterization and assessment of their role in eating behavior.

133 **Immature Olfactory Sensory Neurons Provide Complementary Input In The Healthy Olfactory System**

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Adult neurogenesis of olfactory sensory neurons (OSNs) in the rodent olfactory system provides the unique opportunity to understand how new neurons functionally integrate into existing circuitry and contribute to behaviors. Immature OSNs express odorant receptors (ORs), form dendritic knobs with short cilia, and project their axons into the olfactory bulb (OB) where they form functional synapses. Furthermore, immature OSNs respond selectively to odorants and exhibit graded responses in a higher concentration range than mature OSNs, suggesting that they provide a distinct odor input stream. Finally, in mice that lack mature OSNs, sensory input from exclusively immature OSNs is sufficient to mediate odor detection and discrimination behavior. What remains unknown, however, is how these immature OSNs contribute to odor-guided behavior in the healthy, intact olfactory system. Here we show, using male and female mice, that chemogenetically silencing immature OSNs impairs odor detection ability without affecting their odor discrimination ability. Furthermore, silencing immature OSNs reduced odor-evoked responses in OB neurons based on immediate early gene expression. Finally, silencing immature OSNs reduced the amplitude of odor-evoked dendritic calcium responses in OB output neurons in vivo without affecting odor selectivity. Together, these findings suggest that immature OSNs provide distinct odor input that complements mature OSN input to contribute to odor-guided behaviors in the healthy, intact olfactory system.

135 **Evolutionarily Conserved Mechanisms Of Short-Chain Aldehyde Recognition By The Olfactory Receptor Or6B1**

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Animals discriminate odorants through combinatorial activation patterns of olfactory receptors (ORs). Short-chain aldehydes, including acetaldehyde, have characteristic pungent odors and occur widely in environmental and biological contexts. Using a vapor-phase stimulation assay, we previously identified OR6B1 as the only human OR robustly responsive to acetaldehyde and propanal. OR6B1 is broadly conserved among mammals (Niimura et al., *Genome Research*, 2014), and BLAST searches further suggest the presence of orthologs in reptiles and birds, raising the possibility that aldehyde recognition is conserved across vertebrates. Here, we expressed 19 OR6B1 orthologs in a HEK293T-based heterologous expression system and compared their cell-surface localization and aldehyde responsiveness. Functional expression varied markedly among species. The canine OR6B1 ortholog exhibited the highest membrane localization, consistent with enhanced structural stability, and several reptile orthologs also showed robust surface expression. 15 orthologs responded to a panel of linear aldehydes with carbon chain lengths of C2–C7, similar to human OR6B1, and residues surrounding the predicted agonist-binding pocket were highly conserved. In contrast, a tortoise OR6B1 ortholog carrying a single substitution near the pocket did not respond to acetaldehydes, but instead responded to longer-chain aldehydes, indicating a shift in ligand selectivity. OR6B1 orthologs from dolphin and platypus did not show functional agonist responses under our conditions. Together, these results support an evolutionarily maintained role of OR6B1 in short-chain aldehyde detection, particularly in terrestrial vertebrates, while highlighting lineage-specific diversification of expression properties and ligand selectivity.

137 **Tex15 As A Marker Of Transient Multi-Ors Expression In Developing Olfactory Neurons**

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Before establishing singular odorant receptor (OR) expression, olfactory sensory neurons (OSNs) pass through a transient developmental stage in which multiple OR genes are co-expressed within individual cells. The regulatory mechanisms that permit this temporary co-expression remain elusive. Here, we show that this developmental window is associated with a markedly more accessible chromatin state across OR gene clusters, accompanied by binding of key OR transcription factors to many more sites. To interrogate this stage, we generated a new Tex15CreER allele that enables inducible labeling of early OSN progenitors committed to the neuronal lineage but prior to activation of immature neuronal markers such as Ngn-GFP. RNA-seq analysis confirms that this allele labels a population corresponding to immediate neuronal progenitors (INPS), the stage at which OR gene co-expression occurs. ATAC-seq profiling of Tex15CreER labeled cells reveals stage specific chromatin accessibility, including hundreds of sites within OR gene clusters that are significantly more accessible than in mature OSNs. Consistent with this, Lhx2 and Ldb1 transcription factors that regulate OR gene expression occupy many additional binding sites in immature cells. In contrast, Greek Island enhancer elements display a distinct temporal pattern, with weak accessibility in Tex15CreER cells, peak accessibility in Ngn-GFP cells, and reduced accessibility again in mature OSNs. Together, these results indicate that OR gene clusters undergo dynamic chromatin remodeling during OSN differentiation, enabling transient multi-OR expression before the establishment of singular OR choice.

139 **What Do We Really Smell: Real-Time Chemical Sampling At The Olfactory Epithelium**

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Olfactory perception is typically studied under the implicit assumption that the chemical composition and concentration of an odorant at the nasal entrance accurately reflect the stimulus reaching the olfactory epithelium. However, airflow dynamics, mucosal interactions, and physicochemical properties of odors may substantially transform the stimulus before odorant-receptor binding occurs. Here, we introduce a novel approach combining Proton-Transfer-Reaction Time-of-Flight Mass Spectrometry (PTR-TOF-MS) with simultaneous in vivo sampling at the naris and at the human olfactory epithelium to directly characterize the chemical stimulus that reaches olfactory receptors. Using a range of pure odorants, differing in chemical characteristics, we measured real-time odorant concentration at both sampling locations. Preliminary results reveal variance both between recording locations and odorants, indicating that not all odorant molecules reach the receptor surface equivalently. This variance appears to depend on the chemical identity of the odorant, suggesting that physicochemical properties may shape the effective olfactory stimulus. These findings suggest that perceptual or neural differences may arise from peripheral filtering at the level of the nasal cavity and epithelium, prior to any central neural processing. By directly measuring the chemical stimulus at its point of neural transduction, this work opens new paths for investigating how peripheral processes contribute to odor perception, discrimination, and individual variability in olfaction.

141 **Multistep Ligand Association Reveals How Dynamic Extracellular Gating Controls Odorant Agonism And Antagonism In Olfactory Receptors**

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Olfactory receptors (ORs) are class A GPCRs with broad ligand sensitivity, yet the mechanisms governing odorant selectivity and antagonism remain unclear. Using long-timescale ligand-association molecular dynamics simulations combined with Markov state models, Bayesian network analysis, and cell-based assays, we resolve distinct association and intermediate states during ligand entry across OR classes. In the class I receptor OR51E2, propionate (C3) enters via two extracellular routes and first populates a gate-associated intermediate state; productive association requires opening and re-closure of an ECL2–ECL3 gate. Simulations predicted that heptanoate (C7) preferentially stabilizes the same intermediate gate-associated state, reducing the probability of C3 reaching the associated state; competition assays explain our previous C7 antagonism observations. In the class II receptor OR1A1, hydrophobic ligands associate predominantly through membrane-facing transmembrane pathways. These findings identify ligand-entry intermediates, state-transition probabilities, and gate dynamics as key determinants of OR selectivity and antagonism.

143 **Odor Stimulation In The Mouse Olfactory Epithelium Promotes Transit Amplification Within A Subset Of Neuronal Lineages**

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In mice, olfactory sensory neuron progenitors undergo a variable number of cell divisions before differentiating and selecting for expression 1 out of ~1,200 odorant receptors, which define the neuron's subtype. The process of olfactory sensory neurogenesis has long been assumed to be purely stochastic with respect to subtype. In apparent conflict with this, our lab has found that the birthrates of specific subtypes are selectively increased following exposure to discrete odors that stimulate those subtypes. The mechanism by which this process occurs is unknown. We hypothesize that neural progenitors can be predisposed towards specific subtype fates and can be amplified via cell division due to signals from odor-stimulated neurons, accelerating the birthrates of those subtypes. If this is true, we predicted that odor deprivation should selectively reduce the number of cell divisions observed within a subset of neural lineages. To test this, we first assessed the effects of unilateral naris occlusion on the size distribution of lineages using a Confetti x Kit-CreERT2 mouse model to induce the expression of 1 of 4 fluorescent reporters in neural progenitors and their progeny. As predicted, we observed that odor deprivation decreased the proportion of lineages with large numbers of neurons but did not change the total number of lineages. We next assessed the effects of naris occlusion on how long progenitors undergo transit amplification using a dual thymidine analogue approach. We observed that odor deprivation reduced the proportion of progenitors that continued to divide for at least 48hrs. Our findings support a model where odor-derived signals cause progenitors with pre-disposed subtype fates to undergo more rounds of division, leading to selective increases in the birthrates of these subtypes.

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

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Neurogenesis occurs throughout life in the mammalian olfactory epithelium. In mice, each olfactory sensory neuron precursor selects for expression a single olfactory receptor gene, out of ~1200 possibilities, which determines the mature neuron's subtype. We have found that odor stimulation can accelerate birthrates of specific neuron subtypes, which challenges the established model that olfactory neurogenesis is stochastic with respect to subtype. To explain these findings, we hypothesize that upon stimulation, neurons of some subtypes can signal to progenitors with predisposed subtype fates to selectively 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 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 unknown function that is closely homologous to a protein known to bind complement components. To test whether *Zpld2* plays a role in stimulation-dependent neurogenesis, we generated a *Zpld2*-null mouse. Using scRNA-seq, we found preliminary evidence that *Zpld2*-expressing neuron subtypes undergo stimulation-dependent neurogenesis and that this phenomenon is attenuated in *Zpld2*-null mice. These findings have been validated using EdU-birthdating combined with both RNA-FISH and snRNA-seq. Additionally, RNA-seq based analyses revealed a down-regulation of genes involved in neurogenesis and an up-regulation of genes involved in complement activation in *Zpld2*-null epithelia. These findings suggest a model in which, upon odor stimulation, neurons that express *Zpld2* signal to progenitors, possibly *via* complement components, to promote the neurogenesis of specific neuron subtypes.

149 **Neurogenesis In The Olfactory Epithelium Of Adult Zebrafish Following Olfactory Bulb Lesions**

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Zebrafish (*Danio rerio*) are one of the few vertebrates that can repair brain lesions and generate new neurons (i.e., neurogenesis) throughout their lifespan. In particular, the olfactory system, consisting of the olfactory bulb (OB) and the olfactory epithelium (OE), exhibits extensive neuroplasticity, and repair mechanisms – including neurogenesis – in response to damage. The OE has two stem cell populations that are responsible for constitutive turnover and post-damage regeneration of olfactory sensory neurons (OSNs): and globose basal cells (GBCs) and horizontal basal cells (HBCs),), respectively. While it is known that HBCs are dormant and that direct injury to the OE activates their proliferation, less is known about their role in regenerating the OE after damage of the OB. To study this, in this work we use a model of retrograde degeneration of the OE by excitotoxic lesions in the OB using quinolinic acid (QA) in adult zebrafish. We have established that these lesions cause neurodegeneration in the OE and olfactory functional deficits. Neurogenesis supports recovery by 21 days post-lesion (dpl). In this work, we study recovery and regeneration processes taking place during early post-lesion recovery at 1-, 6-, 24-, and 72- hr post lesion (hpl). We performed immunohistochemical examinations of the olfactory epithelium and assessed markers of cell proliferation, stem cell activation, and neurogenesis. Our results provide a comprehensive time-course characterization of post-damage cell proliferation and neurogenesis in the olfactory epithelium of adult zebrafish. This work contributes to the understanding of basic biological mechanisms underlying neurogenesis in adult vertebrates, with the potential to inform therapeutic strategies to alleviate olfactory dysfunction in human patients.

151 **Subpopulations Of Gustatory Neurons Differ In Their Sensitivity To Bdnf**

Mara J. Stout, Alvine J. Smith, Robin F. Krimm
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Peripheral taste neuron survival and targeting is dependent on expression of neurotrophic factors such as brain-derived neurotrophic factor (BDNF). When BDNF is overexpressed (OE) in basal epithelium of tongue and skin, the number of neurons increases in the geniculate ganglion, but in the tongue these neurons fail to innervate the correct location. Taste neurons are genetically and functionally diverse, and genetic subpopulations could vary in the responsiveness to BDNF. To determine if genetic populations are impacted differently by BDNF overexpression, we investigated the defined proenkephalin (Penk+) expressing population and compared results to the full population defined by expression of the transcription factor paired like homeobox 2B (Phox2b+) in wildtype and OE mice. We found that the number of Penk+ neurons decreased in OE mice ($p<0.05$) whereas the Phox2b+ neurons remained unchanged. We then hypothesized that another genetic subpopulation increases in OE mice, but so far, have found no such population. The decrease in Penk+ geniculate neurons could be due to disrupted target innervation. Consistent with this possibility, by P60, innervation of fungiform taste buds by Penk+ neurons is disrupted when compared to Phox2b+ neurons. Specifically, the percentage of taste buds innervated by Penk+ fibers decreases in OE mice ($p<0.05$) whereas Phox2b+ innervation remains unchanged. In addition, the volume occupied by Penk+ fibers in the taste bud decreased significantly ($p<0.05$) in OE mice compared to controls. Whereas the Phox2b+ nerve fiber volume did not decrease. Our data suggests that subpopulations of taste neurons are impacted differently by BDNF overexpression. Thus, different gustatory neuron types are regulated differentially by developmental factors.

153 **Immune Response Dynamics In The Anterior Taste Field After Nerve Injury**

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Damage to the chorda tympani (CT) nerve through trauma or experimental nerve axotomy results in the

degeneration of anterior taste buds and taste loss. IL-1R and ligands IL-1a and IL-1b are widely expressed in taste receptor cells and surrounding epithelium, gustatory neurons, and infiltrating immune cells. Our previous work demonstrated that IL-1 receptor (IL-1R) signaling is required for taste bud regeneration and the recovery of taste function. However, little is known about changes in immune cell populations in the anterior taste field after experimental axotomy in the absence of IL-1R signaling. To test this, we performed unilateral CT sectioning in *Il1r* KO or wild-type mice. We found that CD45+ immune cells, CD68+ and CD206+ M2-like macrophages are significantly increased near anterior taste buds at day two post-injury in WT mice but not in *Il1r* KO. By day 5 or later at day 56-60, these immune cell types were at baseline levels in both strains, indicating that immune responses to injury were suppressed rather than delayed in the absence of IL-1R signaling. However, taste buds degenerated at similar time points in both strains. These results suggest that delayed taste bud degeneration in *Il1r* KO mice is not the primary reason for later functional deficits, though other unidentified immune and mesenchymal cells may have roles that have yet to be elucidated in the injured peripheral taste system.

155 **Tnf/Tnfr1 Signaling Mediates Inflammation-Induced Remodeling Of Gustatory Innervation**

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A number of inflammatory conditions, including infections and injury, are associated with taste alterations that diminish quality of life and contribute to depression and malnutrition. Despite this clinical significance, effective treatments for taste disorders remain limited due to an incomplete understanding of the relationship between inflammation and gustatory dysfunction. Current literature emphasizes changes in taste receptor cell turnover and function. However, the effects of inflammation on gustatory innervation are less understood. Here, we investigated how inflammation, modeled by lipopolysaccharide (LPS), alters gustatory innervation through tumor necrosis factor (TNF) signaling. Using immunohistochemistry, we quantified nerve fiber volume, TNF expression, and taste bud volume in fungiform papillae at 1 and 4 days following LPS treatment. LPS significantly increased gustatory nerve fiber volume from 1800 μm^3 per bud to 2500 μm^3 per taste bud by day 4. TNF expression, assessed by fluorescent intensity, was also significantly upregulated in the taste bud at day 4 post-treatment. To determine whether TNF mediates this increased innervation pattern, TNF-knockout and TNFR1-knockout mice were treated with LPS and assessed for alterations in nerve fiber volume using immunohistochemistry. Preliminary findings indicate that mice lacking TNF or TNFR1 failed to exhibit the LPS-induced increase in gustatory innervation observed in wild-type controls. Together, these results suggest that TNF/TNFR1 signaling is required for inflammation-induced remodeling of taste nerve fibers. These findings establish a mechanistic link between inflammatory signaling and gustatory innervation and identify TNF/TNFR1 as a potential mediator of inflammation-driven taste alterations.

157 **Trpm8-Mediated Cool-Induced Analgesia In A Mouse Model Of Chemesthetic Oro-Trigeminal Pain**

Chris Brooks, Christian Lemon
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Transient Receptor Potential Melastatin 8 (TRPM8) is a cool-activated cation channel found in sensory neurons within the trigeminal and dorsal root ganglia (DRG). TRPM8+ DRG neurons have been implicated in cool-induced analgesia, possibly via a gate-control mechanism whereby they block parallel nociceptive signals. However, the existence of a TRPM8-mediated analgesia effect in the oro-trigeminal system has not yet been investigated. Herein, we employed a mouse model of oro-trigeminal pain using the TRP Ankyrin 1 (TRPA1) agonist allyl isothiocyanate (AITC, mustard oil) delivered in a concentration series (30uM, 100uM, 300uM, 1000uM) at 5°C, 15°C, and 35°C in brief access water licking trials using 23 mice (11 C57BL/6J, 12 TRPM8-KO). We hypothesized that C57 mice would show less aversion to the nociceptive AITC at 15°C than the KO mice, but not at 5°C or 35°C due to reduced activation of TRPM8. Wilcoxon rank-sum tests revealed significant between-genotype differences in lick rates in the 300uM-15°C ($p=0.049$) and 1000uM-15°C ($p=0.029$) conditions; in both cases the KO mice drank significantly less AITC than C57 mice. These data support our hypothesis that cool temperatures reduce the aversive effect of noxious AITC in the mouth, and that this effect is diminished in mice lacking TRPM8. TRPA1 is primarily expressed on cells that also express TRP Vanilloid 1 (TRPV1). We theorize that TRPM8+ fibers suppress TRPV1+ nociceptors via a central mechanism, e.g. the gate-control model observed in DRG. We plan to continue with capsaicin, a TRPV1 agonist, to clarify if the TRPM8-mediated cool suppression is indeed acting on TRPV1+ nociceptive fibers. We intend to explore the bitter (but not nociceptive) tastant quinine and TRPM8 agonist menthol to further discern what pathways and receptors may be involved.

159 **Mice That Lack Trigeminal Thermosensory Afferents Retain Sensitivity To Oral Temperatures**

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The transient receptor potential vanilloid 1 (TRPV1) ion channel senses noxious temperatures (>43°C) and chemical stimuli (capsaicin) and is an embryonic marker for all thermosensitive neurons including those expressing TRMP8 and TRPA1. Here, we used a mouse line with diphtheria toxin fragment A (DTA) expressed in all embryonic cells expressing TRPV1 to ablate them. Previous studies have shown that TRPV1 lineage ablation leads to temperature and chemical insensitivity on the extremities (Mishra et al., 2011). However, it is unknown if this leads to trigeminal thermal insensitivity in the oral cavity. To test this, C57BL/6J (n = 9; B6) and TRPV1-DTA (n = 10; DTA) mice were proffered water at a reference temperature (30°C or 35°C) and randomly selected test temperature (e.g., 3°, 15°, 40°, or 43°C) in a fluid temperature controlled brief access licking assay over 11 days. Next, they were exposed to increasing concentrations of Ally isothiocyanate (AITC: 0, 0.003, 0.01, 0.03, 0.1, 0.3, and 1mM) and then capsaicin (0, 0.003, 0.03, 0.06, and 0.1 mM). Results showed that the DTA mice retained sensitivity to oral temperatures with some differences between lines. For example, both B6 and DTA mice preferred 30°C water over warmer temperatures (main effect, $p < 0.05$) whereas water temperatures

less than 30°C were more strongly preferred in DTA mice (interaction, p = 0.013). This result suggests that the DTA group is not insensitive to temperatures exposed to the oral cavity, implying non-trigeminal afferents may participate in oral temperature sensing. We plan to use RNA Scope (In-situ hybridization) to fluorescently label and map the presence or lack thereof of thermoTRP ion channels in the trigeminal ganglion of both groups as well as expand studies with new subject groups.

161 **Determining How The Intranasal Chemesthetic Sensation Of Cocaine Contributes To Addiction**

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Chemosensory perception powerfully influences motivated behaviors. Cocaine, a highly addictive psychostimulant, is primarily taken intranasally – a route of delivery associated with high abuse liability. Intranasal cocaine evokes a nasal sensory experience which likely influences the effects of drugs and possibility drug abuse, yet preclinical models relying on intravenous or intraperitoneal administration do not recapitulate the insufflation of cocaine. Understanding how intranasal cocaine and its nasal sensation impact brain and behavior are both major unknown voids in fully resolving the brain's reward system and how chemosensation impacts drug abuse. Here we report the development of an in-dwelling microfluidic device, the nasal access port (NAP). When implanted upon the nasal bone, the NAP permits access to the nasal epithelium of freely behaving rodents to achieve intranasal delivery of drugs with precise control over volume and dosage. First, we validated that intranasal infusion of cocaine rapidly results in detectable levels of cocaine in the plasma and brain, as well as increases in dopamine levels in the reward system. Next, we found that cocaine-infused mice display hyperlocomotion within just minutes post-infusion. Additionally, we show mice extended effort to acquire cocaine intranasally by engaging in an intranasal drug self-administration paradigm in the absence of instrumental cues, except for the nasal sensation evoked by cocaine infusions into the nasal epithelium. Importantly, we observed a rapid sneeze reflex evoked upon delivery of intranasal cocaine, indicative of the sensory response induced by cocaine agonism. Together, this work begins to establish a pre-clinical paradigm to investigate the role of chemosensation in addiction and what mechanisms are at play.

163 **Chemosensory Erps Suggest Peripherally Driven Olfactory&Ndash;Trigeminal Interactions In Older Adults**

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The olfactory and intranasal trigeminal systems are closely connected and can mutually suppress and/or enhance each other, yet the mechanisms underlying their interaction remain poorly understood and have mostly been examined in young adults, despite age-related changes in both systems. To address this gap, we investigated olfactory–trigeminal interactions in 44 healthy older adults (66.3 ± 4.6 years; 29 women) using chemosensory event-related potentials (CSERPs) and the trigeminal localization task. Phenylethanol (PEA, 45%) and CO_2 (40%) were delivered with an olfactometer under four conditions: pure trigeminal (PT; CO_2), pure olfactory (PO; PEA), ipsilateral co-stimulation (IOT; PEA+CO_2 in the same nostril), and contralateral co-stimulation (COT; PEA+CO_2 in opposite nostrils). Brain responses were recorded with a 64-channel EEG system. LPC amplitudes were larger for all three trigeminal-containing conditions than for the PO condition (all $p < 0.001$), with IOT exceeding PT ($p = 0.028$). Further, for trigeminal-containing conditions, LPC amplitudes positively correlated with performance on the trigeminal localization test. Together, these results highlight the prominent role of trigeminal input in chemosensory cortical processing and suggest that olfactory-trigeminal interactions are driven primarily by peripheral rather than central mechanisms. This study also provides normative CSERP data for healthy older adults.

165 **Individual Variability In Metallic Sensation Is Associated With Transient Receptor Potential Vanilloid 1 (*Trpv1*) Polymorphisms.**

Sasi Tansaraviput, Alissa A. Nolden
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A metallic sensation is a pervasive, aversive sensory defect in divalent salt-fortified foods, yet its physiological mechanism remains unclear. Although often described as a gustatory defect, evidence suggests the involvement of a trigeminal component mediated by *TRPV1*. This study investigated the association between *TRPV1* single-nucleotide polymorphisms (SNPs) and the suprathreshold perception of ferrous sulfate ($FeSO_4$) and copper sulfate ($CuSO_4$). The participants were genotyped for four *TRPV1* SNPs (rs224534, rs222747, rs4790522, and rs8065080). Sensory perception was evaluated across 3 concentrations of both stimuli (0.3, 1.0, 3.0 mM). To account for individual variability, participants were segmented into 3 data-driven clusters: High, linear, and inverse metallic responders. Mixed-model ANOVA was used with genotype, concentration, and cluster as fixed effects. Results revealed a significant effect of the rs222747 on $FeSO_4$ metallic perception ($P = 0.002$), with GG carriers reporting lower intensity than GC carriers ($P < 0.05$). An interaction between genotype and cluster was also observed for rs8065080, though post hoc tests were not significant ($P > 0.05$). For $CuSO_4$, a three-way interaction of the rs224534 was observed ($P = 0.04$); at 0.3 mM, metallic perception was higher in AA than in

GA/GG carriers (P <0.05) within the high-intensity cluster. This indicates genetic modulation is not uniform but phenotype-specific at a certain concentration. These findings support a *TRPV1*-mediated trigeminal component in metallic sensation, suggesting divalent metal salts may engage *TRPV1* differently. The interaction between *TRPV1* polymorphisms and sensory phenotypes underscores the need to account for psychophysical response patterns when elucidating genetic influences on complex oral sensations such as metallic.

167 **Unearthing Chemesthesis And Chemesensory Genes In The Earthworm *Dendrobaena Veneta* With Long-Read Transcriptomics.**

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The unique ecological niche of earthworms necessitates that they be chemosensory and somatosensory specialists. Our previous work has focused on describing the cellular and molecular mechanisms of chemosensation and chemesthesis in the earthworm, *Dendrobaena veneta*. Our molecular and behavioral results provide evidence for functional TRP channels (TRPA1 & TRPM8) that appear to mediate the aversive response to irritants such as AITC, cinnamaldehyde, and menthol. We have also demonstrated that sodium salts are more aversive to earthworms than potassium, calcium, or magnesium salts at equivalent concentrations, and that amiloride-sensitive sodium channels are linked to the perception of sodium salts. Additionally, we have determined that glutamic acid and alanine significantly increase worm feeding rates and have identified homologs of the neuropeptides myomodulin and FMRFamide that alter gastric motility. Building on these studies, we present an improved transcriptome assembly utilizing long-read PacBio RNA-seq data. RNA was extracted from cerebral & segmental ganglia, prostomium (e.g. mouth parts) epithelium, flank epithelium, crop, and gizzard (n=3). Libraries from these samples were sequenced on two PacBio Sequel II flow cells, yielding 14.6 million reads. After the standard circular consensus sequencing pipeline, we generated 4.1 million hifi reads per cell with a mean subread length 1,957bp (N50 2,083bp), yielding approximately half a million unique protein-coding transcripts. Blast annotations of those transcripts revealed 37 unique homologs to G-protein coupled glutamate receptors, 48 TRP channel homologs, 9 transcript Epithelial Sodium Channels (ENaCs) subunits. These data provide a comprehensive resource for identifying novel chemoreceptors and signaling pathways in *D. veneta*.

169 **Structural Exploration Of Musk Recognition And Activation Mechanisms Of Odorant Receptors**

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Odorant receptors (ORs) constitute the largest gene superfamily in vertebrates, enabling the detection of a wide variety of odorants. Recent advances in cryo-electron microscopy have facilitated the structural determination of membrane proteins. However, it is still difficult to solve the OR structures due to their inherent instability and typically low cell-surface expression in a heterologous cell system. As a result, only a few OR structures have been reported to date. The limited structural information hampers our understanding of how ORs recognize various odorants and become activated upon ligand binding. To address this fundamental issue, we took advantage of AlphaFold 3 (AF3), a cutting-edge prediction tool for protein structures and interactions with biomolecules. Validation of AF3 models for ORs allowed us to explore ligand recognition logic of a specific OR and common activation mechanisms of OR family. Regarding ligand recognition, we are focusing on OR5A2, a Class II OR that can recognize multiple classes of musk odorants, and tackling how OR5A2 achieves high specificity while simultaneously accommodating the structurally diverse musk compounds. Site-directed mutagenesis guided by the AF3 binding poses identified critical residues for musk recognition. For the activation mechanism, we compared contact scores of each residue pair between active- and inactive-like AF3 models. This analysis suggests that while the OR family may share the same activation features with non-olfactory Class A GPCRs, it also possesses a unique set of activation residue pairs that reflect OR-specific sequence conservation. This study will provide valuable insights into the molecular mechanisms of odor perception.

171 **Tas1R2-Tas1R3 Receptors Modulate Pancreatic Beta Cell Responses To Increases In Glucose**

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TAS1R2-TAS1R3 taste receptors are often co-expressed with a metabolic signaling pathway (MSP) that includes glucose transport, glucokinase, and intracellular ATP sensing via an ATP-sensitive potassium channel. The co-occurrence of these signaling components has been identified both in taste bud receptor cells of the oral cavity and in pancreatic β cells. However, the functional significance of their co-expression in these sensory tissues remains unclear. We hypothesize that together they serve two functions: a steady state detector of absolute glucose levels as well as a rapidly adapting sensor for bidirectional changes in glucose levels. Here we investigated whether stimulation of pancreatic β cells with adapting exposures to glucose and the TAS1R2-3 antagonists ibuprofen and naproxen would modulate β cell activation, as indicated by a calcium fluorophore Fluo-4 AM in the immortalized rat 832/13 INS-1 β-like cells. This calcium fluorophore signal serves as a proxy to measure insulin secretion. Incubating INS-1 cells in 5 mM glucose and stepping their exposure up to 6 mM

glucose (Δl mM) caused a well-known increment in fluorescence. Incubating INS-1 cells in 10 mM glucose and stepping them up to 11 mM (Δ 1 mM) caused a much larger increment in fluorescence. Thus, a 1 mM increase in glucose yields very different relative responses depending on the level of glucose the INS-1 cells have been incubated. Moreover, incubating INS-1 cells in glucose with the Tas1r2-3 antagonists ibuprofen and naproxen interfered with β cell responses to increases in glucose. We also show that these TAS1R antagonists are not disturbing the fluorophore functionality. These data indicate that the Tas1r2-Tas1r3 receptors on pancreatic β cells are highly modulatory of cellular responses to increases in glucose.

173 **A New Tool To Identify And Pharmacologically Characterize Glp-1 Stimuli**

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Enteroendocrine cells, comprising about 1% of the intestinal epithelium, are specialized cells that sense nutrients and mediate hormone secretion. Among them, enteroendocrine L-cells are responsible for secreting Glucagon-like Peptide-1 (GLP-1), which is essential for regulating appetite and glucose metabolism. GLP-1 promotes insulin secretion from the pancreas, suppresses appetite and contributes to weight loss. To detect GLP-1 secretion from enteroendocrine cell supernatants, we optimized and validated a GLP-1 secretion assay. We employed NCI-H716 and STC-1 cell lines, well-characterized models for human and murine intestinal L-cells, respectively, along with a reporter cell line that expresses the recombinant GLP-1 Receptor in combination with the chAMPion reporter system. Our high-throughput screening (HTS)-grade GLP-1 secretion assay was functionally assessed using carbohydrate stimuli, including fructose. Additionally, by testing specific receptor agonists, we confirmed a role for Bitter Taste Receptor 38 (TAS2R38) and Free Fatty Acid Receptor 4 (FFAR4, also known as GPR120) in stimulating GLP-1 release from NCI-H716 and STC-1 cells, respectively. In conclusion, we developed a powerful tool for identifying and pharmacologically profiling novel GLP-1 stimuli, demonstrating its applicability for the identification of new therapeutic strategies in the treatment of diabetes and obesity.

175 **Melanin-Concentrating Hormone And Orexin Neuropeptides Found To Communicate From The Hypothalamus To The Olfactory Bulb**

Julia J. Won[1], Meizhu Qi[1,2,4], Catherine Rodriguez[1], Douglas A. Storace[1,2,3]
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Olfaction plays a vital role in survival as animals regularly utilize olfactory cues to locate mates, care for young, evade predators, and forage for food. Thus, neural circuits that integrate environmental sensory information with interoceptive cues would facilitate an organism's ability to carry out these functions. Previously, we identified that the hypothalamic input to the olfactory bulb (OB) includes a population of neurons that express the neuropeptide orexin-A. The present study aims to define the genetic identity of non-orexinergic input from the hypothalamus to the OB. We recently reported the presence of melanin-concentrating hormone (MCH) expression in the OB, suggesting that hypothalamic neurons expressing MCH could be a candidate population. To test this possibility, retrograde tracer cholera toxin B subunit (CTB) was injected into the mouse OB, and hypothalamic sections underwent immunohistochemistry for orexin-A and MCH. The number, spatial position, and size of all the labeled neurons in the hypothalamus were subsequently quantified. The hypothalamus included retrogradely labeled neurons that did not express orexin-A or MCH, as well as others that overlapped with orexin-A or MCH (i.e., orexin-A and MCH neurons that project to the OB). Therefore, the hypothalamic input to the OB includes projections from multiple genetically distinct populations of neurons. Further studies are needed to fully map out the genetic identity of the remaining projections from the hypothalamus to the OB and to determine their role(s) in olfactory sensory processing.

177 **Gut&Ndash;Brain Modulation Of Taste After Spinal Cord Injury And Sleeve Gastrectomy: Metabolic State And Select Microbial Contributors**

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Approximately two-thirds of individuals with spinal cord injury (SCI) develop overweight or obesity. Although metabolic surgeries such as sleeve gastrectomy (SG) effectively promote long-term weight loss and improve glycemic control, responses to SG in SCI, particularly regarding diet-driven behavior and sensory processing, remain poorly understood. In this study, male Wistar rats underwent thoracic (T3) contusion or sham surgery, followed by six weeks of high-fat diet (60% kcal from fat) exposure prior to SG. SG reduced adiposity, improved glycemic control, and decreased sucrose preference. Notably, SCI-SG rats exhibited enhanced sucrose-evoked cFos activation in the rostral nucleus of the solitary tract compared with non-SCI SG rats. We further evaluated the contribution of gut microbiota using fecal microbiome transplantation (FMT), comparing autologous and heterologous transplants on taste and metabolic outcomes, including body composition, metabolic rate, and glycemic control. SG-associated alterations in taste responses assessed by using brief-access lick tests, i.e., reduced sucrose licks and changes in salt and sour sensitivity, were partially transferable via FMT, supporting a mechanistic role for the gut microbiome in modulating taste after SG. Taste responses tracked modestly with metabolic state, particularly fat mass, whereas most taxa differentiating SG and FMT groups showed no association with taste. In contrast, a small subset of taxa, including Clostridioides-associated lineages, correlated with taste outcomes. Together, these findings indicate that SG-related taste alterations align with metabolic state

and identify candidate microbes for mechanistic testing and targeted probiotic strategies to improve post-surgical outcomes in SCI.

179 **Disruption Of Taste Cell Renewal In Diet-Induced Obesity**

Sabrina K Choi, Robin Dando
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Diet-induced obesity is associated with reduced taste bud abundance and altered taste function in mice, yet the specific stage(s) of taste cell renewal that is disrupted by obesity remains unclear. Taste buds are continuously renewed through a tightly regulated signaling cascade involving progenitor cell maintenance, cellular proliferation, differentiation into mature taste cells, and programmed cell death. We hypothesize that obesity alters discrete stages of this renewal process, resulting in impaired incorporation of newly generated cells into the taste bud. To test this, we conducted a longitudinal EdU pulse-chase staining and immunohistochemistry study in lean and diet-induced obese mice across a time course of 56 days. Taste bud structure and abundance were assessed using KCNQ1, while proliferative activity and cell-cycle behavior were evaluated with Ki67 and EdU labeling. SOX2 was used to quantify the progenitor pool and progenitor entry into S-phase, and cleaved caspase-3 identified apoptotic events. Multiplex marker combinations (e.g., SOX2, Ki67, and EdU; KCNQ1, Caspase-3, and EdU) were also used to evaluate progenitor activation, cell-cycle exit, differentiation into taste buds, and preferential death of newly generated versus older cells. Using this approach, we aimed to characterize the stage-specific mechanisms by which obesity disrupts taste cell renewal, providing insight into potential strategies to restore taste function in obesity.

181 **Slow-Acting Peripheral Inhibition Underlies The Behavioral Dominance Of Aversive Acidic Odors**

Kay J. Ellison, Isaiah K. Asbed, James M. Jeanne
Yale University, New Haven, CT, United States

Animals often encounter environments containing multiple odors, yet how the nervous system prioritizes them to guide behavior remains poorly understood. Here, we identify a novel form of sensory dominance in *Drosophila melanogaster* in which aversive acidic odors hierarchically control behavioral choice. When forced to choose between equally aversive acidic and non-acidic odors, flies prefer to avoid the acidic odor. Notably, acidic odors override aversion to both innately aversive odors as well as odors rendered aversive through recent learning. This dominance emerges over tens of seconds and occurs only at acidic odor concentrations that are themselves innately aversive. Using *in vivo* calcium imaging, we show that acetic acid suppresses activity in olfactory receptor neurons (ORNs) expressing Orco, which encode non-acidic odors. This suppression occurs on the same slow timescale and with the same concentration-dependence as the behavioral dominance. Interestingly, suppression occurs in both the antenna and the antennal lobe, indicating that acid dominance is implemented within the sensory periphery. In contrast, non-acidic odors have no impact on activity in ORNs expressing Ir8a, which encode acidic odors. Suppression of Orco+ ORNs is propagated to downstream projection neurons, with inhibition in both populations closely matching the temporal dynamics of behavioral dominance. Together, these results reveal that hidden odor hierarchies can emerge during decision-making and can be implemented through asymmetric inhibition between peripheral sensory channels. This represents a previously unrecognized organizing principle in olfaction. Ecologically salient chemical cues can thus shape sensory priority at the earliest stages of the nervous system, prior to higher-order integration.

5:45 - 6:45 PM	Garden Courtyard
Networking Reception	

The Networking Reception is an opportunity for the AChemS community to get together in an informal setting. We will honor the recipients of the Travel Fellowship and then enjoy conversations with junior and senior colleagues. Attendees who signed up for the Mentoring Matrix Program in advance will meet with their Matrix members. There will also be the possibility of joining or creating new Mentoring Matrices on site.

7:30 - 9:30 PM	Sawyer Key
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): Bradley Goldstein

7:30 **Evolutionary Diversity And Function Of Odorant Receptors In Birds**

Robert Driver[1], Mona Marie[1], Hiroaki Matsunami[1], Christopher Balakrishnan[2]

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An incredible variety of chemicals are perceived as smell by animals. To detect this vast range of volatiles, odorant receptors (ORs) have diversified into one of the largest gene families in vertebrates; for example, many mammals have over 1,000 OR genes. Birds, with over 10,000 extant species, inhabit nearly all land environments and exhibit diverse breeding and foraging behaviors yet were long thought to make limited use of olfactory signals. Here, we used genomic and molecular approaches to demonstrate the relevance of the avian olfactory system. We show that, like mammals, bird genomes often contain hundreds – or in some cases, thousands – of intact ORs, including the nocturnal kiwi (*Apteryx manetllii*), which possesses the largest number of ORs known from any animal. The majority of avian ORs belong to a bird-specific expansion known as gamma-c ORs. We found that this expansion was characterized by extensive gene conversion leading to mosaic open reading frames with diverse regions interspersed with regions nearly identical in nucleotide sequence. We show that avian ORs are expressed in olfactory sensory neurons and respond to specific odors *in vitro* and *in vivo*. Notably we identify for the first time ligands for avian ORs documenting both unique function in gamma-c ORs and shared function with a deeply divergent mammal OR. Our findings highlight commonalities between mammals and birds in olfactory system function but also reveal a unique evolutionary feature: the widespread role of gene conversion shaping the majority of bird ORs. Our results challenge prior assumptions and underscore the importance of olfaction in the life history of birds.

7:50 **A Sensory Circuit For Social Learning**

Kara A. Fulton[1], Slater Sharp[1], Gloria DuMaine[1], Sidharth Annapragada[1], Phelipe E. Silva[1,2], Sebastian Kruettner[1,3], Emma Robinson[1,4], Sandeep R. Datta[1]

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In social contexts, mice can learn about the safety of food through an association formed between food odors and the semiochemicals present in the breath or feces of other mice. This behavior is known as the social transmission of food preference and is mediated through the necklace olfactory subsystem via the Guanylyl Cyclase D (GCD) olfactory receptors (Munger et al., 2010). However, it remains unclear how the sensory information encoded by the GCD neurons are transmitted to the rest of the brain and how the olfactory system supports this form of social learning. Through a combination of viral tracing and optogenetics, we have identified a circuit between the GCD projection neurons in the olfactory bulb and basal forebrain which is necessary and sufficient for this olfactory-mediated social learning. The connectivity of the GCD olfactory circuit with the basal forebrain suggests that this network is suited not only for processing social odors, but also for improving learning. Indeed, activation of GCD projection neurons (through odor ligands, optogenetics, or chemogenetics) activates neurons in the basal forebrain and evokes acetylcholine release as measured through fiber photometry or GRIN-based calcium imaging. Collectively, our data suggests that the necklace olfactory system is functionally connected to the cholinergic system that is important for learning and memory. In addition to promoting social learning of food preferences, chemogenetic or optogenetic activation of GCD neurons enhances memory formation during social recognition and novel object tasks and enables optimal spatial navigation in complex environments. We propose that this sensory circuit may have evolved to recruit attention to support learning in a variety of ethological conditions which require flexible behavior.

8:10 **Vector-Based Taste Representations Of Food Odours Predict Appetitive Value**

Putu A Khorisantono[1], Apostolia Filippopoliti[1], Maria G Veldhuizen[2,3], Janina Seubert[1]

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Flavour perception arises from the integration of gustatory and olfactory signals, yet how learned taste-odour associations are represented in the brain and translated into appetitive behaviour remains poorly understood. Our prior work demonstrated that aromas acquire taste-like neural representations through flavour learning: using a flavour-binding paradigm and fMRI, we showed that tasteless aromas evoke activity patterns in the human insular cortex that overlap with those elicited by their paired tastants, particularly in the dysgranular and agranular insula. These findings established a shared and dynamic neural code for taste and retronasal olfaction, providing a cortical mechanism through which aromas acquire consummatory meaning. Building on this neural framework, the present pre-registered study extends taste-odour integration beyond retronasal perception to orthonasal food odours and examines how predicted taste properties modulate food wanting. Healthy volunteers completed a taste-rating session to derive individual sweet and savoury preference, followed by ratings of orthonasally delivered food odours along sweetness, savouriness and wanting dimensions. Mixed-effects modelling predicted odour-elicited food wanting from an interaction between individual taste liking and the expected taste properties of food odours. Moreover, a vector-based representation of odours in sweet-savoury space outperformed a scalar spectral model in predicting appetitiveness, with cross-validated generalisation across participants. Together, these findings link shared taste-odour neural coding in the insula to orthonasal odour-guided appetitive behaviour, highlighting how lifelong associative learning shapes food valuation and suggesting mechanisms through which sensory expectations influence dietary choices.

8:30 **Asymmetric Histone Inheritance Regulates Olfactory Stem Cell Fates During Regeneration**

Binbin Ma[1, 2], Guanghui Yang[1, 2], Jonathan Yao[2], Charles Wu[2], Jean P Vega[2], Gabriel Manske[3], Saher S Hammoud[3], Satrajit Sinha[4], Abhyudai Singh[5], Haiqing Zhao[2], Xin Chen[1, 2]

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The olfactory epithelium (OE) possesses an adult stem cell population, the horizontal basal cells (HBCs), to permit lifelong tissue regeneration. Here we show that HBCs exhibit asymmetric inheritance of histone H4 but not H2A-H2B during OE regeneration in mice. Primary HBC cultures further revealed asymmetric histone inheritance for H3 and H3.3. Upon mitotic exit, asymmetric histone inheritance correlates with asynchronous transcription re-initiation and differential enrichment of p63, a key transcription factor for HBC cell fate. Disruption of asymmetric histone inheritance abolished these asymmetric cellular features and attenuated OE regeneration and smell behavior recovery. Single-cell RNA sequencing of paired HBC daughters in culture further supported asymmetric multilineage cell fate priming. Together, these findings reveal asymmetric histone inheritance in a mammalian adult stem cell lineage and highlight its biological significance in neural tissue regeneration and animal behavior.

8:50 **A Quantitative Perceptual Framework For ReconstructiNg Complex Food Odors**

Xuebo Song[1], Christiane Danilo[1], Robert Pellegrino[1], Joel Mainland[1, 2]

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Odor perception plays a central role in food preferences, yet we lack a quantitative framework for understanding how complex food odors emerge from molecular mixtures. Odor mixtures have been reported to exhibit qualities distinct from their individual components, suggesting that interactions between odorants dominate mixture perception. However, linear models that assume independent and additive perceptual contributions from component molecules have performed surprisingly well at predicting odor mixture character in human behavioral studies using mixtures of up to 10 components. To test how well linear models can reproduce complex food percepts, we collected descriptive ratings for 24 foods alongside their published Sensomics-based reconstructions (GC-MS analysis followed by sensory testing). Using greedy search within a linear perceptual framework, we iteratively selected components from a database of ~700 individual stimuli to identify component mixtures minimizing perceptual distance to each target food and best approximating each food's sensory profile. For 18 of 24 foods, these perceptually-optimized mixtures matched the target food more closely than the Sensomics reconstructions, despite using no information about the foods' chemical composition. These results demonstrate that odor components combine predictably even in complex foods, extending the validity of linear mixture models from simple laboratory mixtures to real food systems. A perceptual framework for olfactory mixture design offers a complementary approach to analytical methods, enabling food odor reconstruction from any available ingredient library.

9:10 **Connectomic Mapping Of Pharyngeal And Gut Sensory Circuits In Adult *Drosophila***

Dimitrios S. Giakoumas[1], Julia M. Zhu[1], Alaina Jamal[2], Zepeng Yao[1]

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Feeding is regulated by both external sensory signals, such as taste, and internal sensory signals originating from the pharynx and gut. The recent completion of the Full Adult Fly Brain (FAFB) connectome presents an exciting opportunity to map these sensory inputs and their downstream circuits. While the external gustatory receptor neurons (GRNs) have been relatively well characterized, the internal pharyngeal and gut sensory neurons remain less understood. Here, we systemically identify their axonal projections in the FAFB connectome and examine their downstream circuits. We find that the stomodeal nerve, which carries afferent signals from the

gastrointestinal tract to the brain, contains multiple types of sensory axons with distinct morphology and downstream connectivity. In addition, we identify sensory axons derived from different pharyngeal sense organs and find that chemosensory and mechanosensory neurons project to distinct regions of the subesophageal zone. Characterization of the second- and third-order neurons reveals the brain regions that receive inputs from pharyngeal and gut sensory neurons. Interestingly, a subset of these internal sensory neurons forms monosynaptic connections with various motor neurons and endocrine cells, suggesting that internal signals from the gut and pharynx may directly drive feeding-related motor programs and endocrine functions. Together, this study provides a foundation for further analysis of feeding-related internal sensory circuits and may offer insights into how external and internal sensory signals are integrated to regulate feeding behavior.

Friday, April 24, 2026

7:30 - 9:00 AM	Pavilion/ Pavilion Lawn
Continental Breakfast	

8:00 - 10:00 AM	Pavilion
Poster Session III	

200 **Salivary Proteins In Bitterness Perception In Humans**

Yashmita Grover[1], John N. Coupland[1], John E. Hayes[1,2], Neela H. Yennawar[3]
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Bitterness is an aversive taste that can limit the acceptance of nutritionally beneficial foods like vegetables. Its perception begins with the dissolution of bitterants in saliva before they can activate taste receptors. Saliva is composed of water, ions, and critically, proteins, which may interact with bitterants in the oral cavity. Salivary proteins could influence taste by interacting with either taste receptors or chemical stimuli; to date, most evidence comes from animal studies, leaving the contribution of salivary proteins to bitterness perception in humans incompletely understood. Here, we explored binding interactions between human salivary proteins and quinine as a step toward understanding their potential role in bitterness perception. Saliva from 46 healthy volunteers was pooled and separated (3 kDa filter) into low and high molecular weight protein fractions. Protein-unbound quinine was quantified in whole and fractionated saliva using fluorescence spectroscopy, and binding was further characterized using isothermal titration calorimetry and analytical ultracentrifugation. The proportion of unbound quinine decreased with increasing protein concentration (to 59% at 0.6 mg/mL protein). Salivary proteins showed higher binding coefficient and reaction enthalpy, binding quinine comparably at 4.3X lower protein concentration than sodium caseinate, a food-grade protein previously studied by our team. Low molecular weight salivary proteins and peptides were particularly active, displaying the highest binding coefficient and enthalpy. This was further supported by the presence of protein-quinine complexes at higher sedimentation coefficients. This study demonstrates that human salivary proteins bind quinine, providing a foundation for future research into their role in bitterness perception.

202 **Assessing The Generalizability Of Salivary Proteins Across Bitter Compounds**

Kamila D. Nixon[1], Verenice Ascencio Gutierrez[1], Samantha L. Brooker[1], Ann-Marie Torregrossa[1,2]
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Our lab has demonstrated that 1) rats increase intake of bitter diets (e.g. quinine) after repeated exposure, 2) dietary exposure to the bitter can drive changes in salivary proteins (SPs), 3) these SPs decrease the bitterness of the same stimulus. We do not know if these changes in SPs will generalize to acceptance of other bitter foods which may be unsafe to consume. Here, we asked if diet-induced changes in SP expression, which increase the animal's acceptance of safe bitter substances, will increase acceptance of a similar but bioactive stimulus. We chose to begin by comparing quinine and caffeine which are alkaloids with different post-oral actions. We used brief-access tests to measure taste-driven responses to quinine and caffeine, before and after SPs were manipulated by diet exposure. Rats that were fed a 0.375% quinine diet to increase SP production licked more to quinine ($p = 0.04$) but not to caffeine during testing ($p=0.23$). However, those that were fed a 0.3% caffeine diet increased acceptance of both caffeine ($p = 0.03$) and quinine ($p = 0.01$) solutions in brief-access tests. SP profiles appear to partially overlap after exposure to these diets. More work needs to be done to identify overlapping proteins. However, these data suggest that even if SPs are present, if a diet has an additional post-oral action animals will continue to show caution.

204 **Taste-Associated Lingual Salivary Gland Ducts Participate In Mucosal Immune-Surveillance**

Abdul Hamid Siddiqui, Salin Raj Palayyan, Sunil K. Sukumaran
Nutrition and Health Sciences Department, University of Nebraska, Lincoln, NE, United States

The oral cavity is a major portal for microbial entry, and the oral microbiome is among the most diverse microbial ecosystems in the body, second only to the gut. While salivary secretions provide a key antimicrobial barrier via enzymes such as lysozyme, the epithelial structures that deliver these secretions may also contribute directly to mucosal defense. The von-Ebner's gland (VEG), a relatively less studied lingual minor salivary gland, drains into the circumvallate papillae through dedicated ductal networks. Salivary and lachrymal ducts are known to function as immune-surveillance sites, and the VEG ducts, located at the interface between the taste

buds and the underlying secretory and immune compartments are uniquely positioned to fulfil this role. Using single-cell RNA sequencing of murine taste papillae, we identified a distinct duct cell gene expression program characterized by expression of immune-surveillance pathways for microbial sampling such as phagocytosis and transcytosis, first identified in microfold cells in the mucosa-associated lymphoid tissues. The expression of genes involved in these pathways was confirmed using RNAscope and immunohistochemistry, and the ability of duct cells to transcytose microbes was demonstrated using fluorescently labelled *E.coli*. Collectively, these findings support a model in which VEG ducts are not passive channels but specialized epithelial sentinels that may sample the luminal content and contribute to mucosal immunity within the circumvallate papillae microenvironment. Defining duct-mediated immune surveillance mechanisms may reshape our understanding of oral mucosal defense and reveal new epithelial targets for modulating host microbe interactions in the oral cavity.

206 **Individual Differences In Salivary Ion Composition And Its Association With Oral Glucose Sensitivity**

Alexa J Pullicin[1], Yixin Jia[1], ASM Saem[2], Juyun Lim[1]

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Saliva contains a variety of ions that may play important roles in taste function, yet little is known about their composition, intra- and interindividual variability, or contributions to taste perception. Here, we examined individual differences in salivary sodium (Na^+), potassium (K^+), magnesium (Mg^{2+}), and calcium (Ca^{2+}) concentrations across days and metabolic states (fasted and fed), and their potential relationships with oral glucose detection thresholds (DTs). All salivary ion concentrations exhibited large interindividual variability but were highly consistent within individuals across fasted and fed states (N=33; Na^+ r=0.70, p<0.00001; K^+ r=0.53, p=0.002; Mg^{2+} r=0.52, p=0.002; Ca^{2+} r=0.76, p<0.00001). When a subset of individuals (N=14) were tested on two separate days, fasting salivary Na^+ , K^+, and Mg^{2+} concentrations showed moderate positive correlations (Na^+ r=0.58, p=0.03; K^+ r=0.52, p=0.06; Mg^{2+} r=0.69, p=0.0006), but Ca^{2+} did not (r=0.23, p>0.05). Notably, higher fasting salivary K^+ concentrations were associated with lower oral glucose DTs, indicating greater glucose sensitivity (r=-0.45, p<0.01). In contrast, fasting salivary Na^+, Mg^{2+}, and Ca^{2+} concentrations showed no relationship to DTs (r=0.08, r=-0.26, and r=-0.27, respectively; all p>0.05). These findings demonstrate that salivary ion composition is generally stable within individuals across days and suggests a potential link between salivary K^+ and oral glucose sensing. Ongoing analyses are examining the mechanistic basis of this relationship and its implications for glucose taste sensitivity.

208 **Salivary Protein Profile Changes Taste Guided Behaviors Independent Of Diet.**

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Bitter foods are often avoided as bitterness is associated with potential toxicity. Our laboratory has demonstrated that diet alters salivary protein (SP) expression, and that these proteins, in turn, increase acceptance of the bitter diet. In the current experiment, we explored which salivary proteins appear to contribute to changes in dietary acceptance. Male Long Evans rats were given a non-bitter control diet, a 0.375% quinine diet, or a 3% tannic acid diet ad libitum. Animals also underwent brief-access taste testing (Davis-Rig) to sucrose and quinine solutions after two weeks of diet exposure. Saliva was collected at the conclusion of the study and analyzed using gel electrophoresis. All animals independent of diet were entered into a mixed statistical model. 14kDa, 18.5kDa, 19kDa, 23kDa, 53kDa, 75kDa, and 215kDa proteins correlated to EC50 (p's<0.05), which represents the concentration that is halfway to the animals' asymptotic licking. We then identified the 15 animals with the highest EC50 (least sensitive to quinine) and the 15 animals with the lowest EC50 (most sensitive to quinine). These groups differ at the 18.5kDa, 23kDa, 53kDa, 75Kda, 100kDa, and 215kDa bands (p's<0.05). The animals fed quinine and some tannin animals make up the majority of the less sensitive group (high EC50), although a few control animals also had high protein expression and low sensitivity and therefore were included in this group. This distribution of the control animals across the test groups highlights individual variation in either protein expression or sensitivity to initiate up regulation. We are awaiting LC-MS-based proteomic identification and quantitation of these samples.

210 **Sour Suppresses Sweet, Salty, And Bitter: Does This Begin In The Taste Bud?**

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Citric acid is known to suppress sweet, salty, and bitter taste. This likely underlies the culinary wisdom of adding a twist of lemon to balance flavors. One proposed mechanism is that acid-sensing Type III taste bud cells release inhibitory transmitters, including serotonin (5HT), that dampen neighboring taste cell responses. We tested this notion by recording activity of gustatory neurons in the mouse geniculate ganglion. These neurons carry the output from taste buds of the anterior tongue and palate into the hindbrain. Using *in vivo* Ca^{2+} imaging in mice that express GCaMP6 in sensory neurons, we measured ganglion neuron responses ($\Delta F/F$) to single tastants and to mixtures containing acid. Adding 10 mM citric acid or HCl to sucrose, NaCl, or a bitter mixture significantly reduced ganglion neuron responses for each tastant from control levels (no acid) to 36% (71 neurons, p<0.0001), 63% (26 neurons, p<0.0001), and 26% (27 neurons, p=0.001), respectively. Next, we

manipulated 5HT levels in taste buds. Increasing the 5HT content of taste buds by injecting mice with 5-hydroxytryptophan (5HTP) doubled the 5HT-immunopositive cells in taste buds (37%→76%, 502 cells, p=.002) and enhanced acid-mediated inhibition of sucrose responses (36%→7% of control, 58 neurons, p=0.027). Conversely, reducing 5HT by treating mice with parachlorophenylalanine (PCPA) weakened acid inhibition of sucrose responses (36%→61%, 71 neurons, p=.0003). Inexplicably, PCPA did not alter the incidence of 5HT-immunopositive taste bud cells. These data support the conclusion that acids suppress other taste qualities in part through 5HT-mediated paracrine inhibition within taste buds. The findings emphasize that some degree of signal processing takes place in these peripheral sensory organs.

212 **Evidence For A Glucose-Specific Taste Pathway That Triggers Insulin Release In NaÏVe B6 Mice**

John I. Glendinning[1], Natalie Ashkar[1], Kiriaki Georgiou[1], Ashley Guardado[1], Julia Istefanos[1], Nidhi Khanchumarti [1], Yixin Jia[4], Janet Liu[1], Kathryn Medler[3], Laura Mittelman[1], Sarah Nordlicht[1], Clara Resnick[1], Abigail Spingarn[1], Anne-Marie Torregrossa[2]

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The cephalic-phase insulin response (CPIR) is elicited by food-related stimuli. It causes a rapid rise in plasma insulin, and promotes the disposal of glucose during and after meals. Here, we conducted 6 experiments to explore the mechanistic basis of a specific type of CPIR, which is elicited by the ingestion of solutions containing glucose or glucose-containing carbohydrates in sugar-naïve mice. First, we used IP_3R_3 receptor knock-out (KO) mice to determine whether this receptor—a critical component of the T1R2+R3 sweet taste pathway—is necessary for D-glucose to elicit a CPIR. We found that deletion of the IP_3R_3 receptor had no impact on the glucose-induced CPIR. Second, we asked whether D-glucose elicits a peripheral taste response in IP_3R_3 receptor KO mice. We observed a chorda tympani nerve response to lingual stimulation with D-glucose, but not sucrose, fructose or saccharin. Third, we determined whether flushing the mouth with D-glucose was sufficient to elicit a CPIR in B6 mice. We found that flushing with D-glucose but not fructose elicited a CPIR. Fourth, we asked whether stimulation of the T1R2+R3 taste pathway with saccharin enhanced the CPIR to D-glucose. We did not observe any enhancement. Fifth, we reasoned that if the CPIR is mediated by a glucose-specific taste pathway analogous to the one in pancreatic beta cells, then it should be triggered by ingestion of D-glucose but not L-glucose or isomaltulose. As predicted, D-glucose alone triggered a CPIR. Sixth, given that D-glucose evokes a salient odor in mice, we predicted that olfactory input may contribute to the glucose-induced CPIR. Olfactory impairment had no impact. These results provide multiple lines of support for the hypothesis that the glucose-induced CPIR is initiated by activation of a glucose-specific taste pathway.

214 **GA_Q Protein-Coupled Receptors And Store-Operated Calcium Entry Via Orai Channels Might Be Involved In The Lingering Perception Of Astringency**

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The mechanism behind the dry and lingering sensation, known as astringency, that occurs after consuming foods rich in polyphenols is not yet fully understood. Although various theories on how astringency might be perceived mechanistically have been proposed, it is still unclear whether, and if so, which GPCRs, and/or ion channels, are involved in astringency. Our hypothesis is that GPCRs coupled to $G\alpha_q$ are activated by astringent compounds to induce a Ca^{2+} mobilization and that store-operated calcium entry (SOCE) via Orai channels, inducing a longer-lasting Ca^{2+} influx, results in the lingering effect of astringency. To address this, we performed Ca^{2+} imaging experiments, using the puckering astringent compounds epigallocatechin gallate (EGCG) and tannic acid (TA), the velvety astringent rutin, and the non-astringent and bitter-tasting quinine in the human tongue cell line HSC-3, a widely used surrogate model for investigating astringency. By applying the $G\alpha_q$ inhibitor FR900359, the Ca^{2+}-signal was reduced only for EGCG, TA, and rutin, but not for quinine. Furthermore, the lasting Ca^{2+}-signal of EGCG and TA was blocked by the Orai channel inhibitor Synta66, whereas no reduction was detected for rutin and quinine, as confirmed by knock-down experiments. This indicates that SOCE might be involved in the puckering and lingering perception of astringency but not in the short-lasting and velvety astringency, as further evidenced by sensory studies showing that EGCG and TA are perceived more lingering than rutin (p <0.05) at perception thresholds. To summarize, these results provide evidence that astringency may be perceived through $G\alpha_q$ protein-coupled receptors and that the lingering effect can be attributed to the involvement of SOCE via Orai channels.

216 **The Kokumi Taste Characteristic Of Mayonnaise Is Due To Its Egg Yolk Content And The Length Of Its Storage Period**

Mari Yoshida[1], Yoshiko Tamura[1], Takuya Yanagisawa[1], Takumi Misaka[2]

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Kokumi is a taste long cherished in Japanese cuisine, imparting depth and complexity. Japanese mayonnaise varieties containing more egg yolk are known to have pronounced kokumi. Recent studies have revealed that

calcium-sensing receptors (CaSR) are involved in the sensing of kokumi substances. We previously conducted CaSR activity and sensory evaluations on molecular weight-fractionated mayonnaise extracts, demonstrating that low-molecular-weight peptides under 1000 Da contribute to kokumi flavor in mayonnaise. In this study, we prepared mayonnaise samples with different egg yolk contents and storage periods (6 and 10%, 35°C × 0 and 2 weeks; 14%, 35°C × 0, 2, 6, and 12 weeks). We evaluated the response of CaSR-expressing cells using a Ca^{2+} flux signaling assay. Gel filtration chromatography and quadrupole-Orbitrap hybrid mass spectrometry were performed to evaluate the yields and compositions of the low-molecular-weight peptides. All samples stored for ≥ 2 weeks activated CaSR in a concentration-dependent manner, and this activity was inhibited by the CaSR antagonist, NPS-2143. CaSR response values were positively correlated with egg yolk contents and storage periods. Similarly, low-molecular-weight peptide production were positively correlated with egg yolk contents and storage periods ($p<0.001$, $r>0.90$). A total of 474 mono- to tetrapeptides showed a positive correlation with CaSR response values ($p<0.05$, $r>0.80$). The results demonstrated that higher egg yolk contents and longer storage periods led to the generation of multiple low-molecular-weight peptides. These peptides activate CaSR, contributing to the kokumi characteristic of egg-yolk-type mayonnaise. Since kokumi have taste-enhancing effects, the use of egg-yolk-type mayonnaise may offer health benefits by reducing salt intake.

218 **Identification Of The Bitter Taste Receptors For Tuberculosis And Anti-Infection Medications**

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Bitterness is a complex human taste sensation, mediated by 25 functional bitter taste receptor genes (TAS2R) that collectively detect thousands of structurally diverse bitter compounds (Meyehof et al., 2010). These G-protein-coupled receptors, expressed on taste cells, initiate afferent signaling to the brain in response to bitter stimuli (Bachmanov and Beauchamp, 2007). Few effective strategies exist to block the bitterness of essential medications, contributing to poor adherence in vulnerable populations. Prior work identified a subset of the 25 TAS2Rs as mediators of the bitterness of antiviral, antischistosomal, and antimalarial active pharmaceutical ingredients (APIs). Tenofovir alafenamide (TAF), an HIV treatment, activates TAS2R1, TAS2R8, TAS2R14, and TAS2R39 (Schwiebert et al., 2021; Caronia et al., 2023). However, the TAS2Rs underlying the bitterness of tuberculosis (TB) drugs remain largely uncharacterized. We hypothesize that TB drugs and other essential APIs elicit bitterness through a similar set of TAS2Rs. To test this, 17 APIs used for TB and other infectious diseases were screened for activation of all 25 TAS2Rs using cell-based functional assays. HEK293 cells were transiently transfected with individual TAS2Rs and the chimeric G protein Gα16-gust44 to couple receptor activation to calcium mobilization. For 8 APIs, solubility issues, endogenous activity, or lack of bitterness at tested concentrations prevented assessment of TAS2R activation. The remaining 9 APIs activated a subset of TAS2Rs, most frequently TAS2R1, TAS2R8, TAS2R14, and TAS2R39; TAS2R10 and TAS2R46 also responded to some compounds. These findings suggest a small receptor subset drives bitterness across a variety of TB and anti-infection medications, informing strategies to improve drug palatability and compliance.

220 **Calca Gene-Derived Peptide Expression In The Murine Taste System**

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The *Calca* mRNA undergoes alternative splicing to generate either preproCGRP or preprocalcitonin. The proteolytic processing of preprocalcitonin generates bioactive peptides - procalcitonin, calcitonin, and katacalcin, while CGRPα is generated from preproCGRP. The cellular origins, processing, and activity of *Calca*-derived peptides within the taste system remain poorly defined. Previous studies indicated that CGRPα may regulate ATP release from type II taste cells. CGRPα signals via the CGRP1R, while procalcitonin can also bind CGRP1R and antagonize CGRP signaling. We aimed to uncover how *Calca* gene-derived peptides and CGRP1R signaling are organized within the taste system. Using integrated single-cell and bulk RNA sequencing of murine taste papillae, we uncovered a striking cellular segregation of transcripts for *Calca* and their receptors. Preprocalcitonin transcripts-but not CGRP-were selectively expressed in *Tas1r3*+ type II taste cells. In contrast, *Calcrl* and *Ramp1*, but not *Calcr*, were enriched in stem/progenitor and type I taste cells within the circumvallate papillae, as well as in lingual mesenchymal fibroblasts. Analysis of geniculate and nodose-petrosal ganglia revealed robust expression of *Cgrp* and *Cgrp1r* subunits, but not procalcitonin or *Calcr*. The expression validation using qPCR, RNAscope, IHC and western blotting, indicated that procalcitonin but not calcitonin is produced by type II taste cells. These findings reveal a unique distribution of Calca- derived ligands and their receptors in the taste papillae-innervating neurons and resident epithelial cells. We propose that the reciprocal regulation of CGRP1R by CGRPα and procalcitonin may coordinate taste transduction, epithelial regeneration, uncovering new dimensions of neuroepithelial communication in the gustatory system.

224 **From Cage To Lab To Clinic: Treating A Human Psychiatric Condition Using A Social Chemosignal First Identified In Mice**

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Hexadecanal (HEX) may be a conserved mammalian-wide social chemosignal (Klein et al., 2015; Hoppe et al., 2006). In humans, HEX reduces reactive aggression and startle in men (Mishor et al., 2021; Endevelt-Shapira et al., 2018). To test the hypothesis that HEX impacts autonomic physiology, 55 adults (31 women) completed three counterbalanced sessions on separate days under HEX (in an odor-masking carrier), lavender, and carrier alone. During each session, participants viewed a neutral film while receiving 20 acoustic probes. Eyeblink EMG, electrodermal activity (EDA), ECG, and emotion ratings were recorded. Lavender was rated as substantially more pleasant, intense, and familiar than both HEX and control (all Holm-corrected $p<10^{-9}$),

whereas HEX differed only weakly from control, confirming its perceptual subtlety. Despite this, HEX selectively altered autonomic physiology. In women, HEX significantly reduced startle magnitude and EDA responses relative to control (both FDR-corrected p<.03), consistent with reduced sympathetic reactivity. In men, HEX did not alter startle or EDA but produced a marked decrease in tonic heart rate together with increases in heart-rate variability (RMSSD and pNN50; all FDR-corrected p<.05), indicating enhanced parasympathetic dominance. Subjectively, HEX selectively increased feelings of safety in men (FDR-corrected p=.031). Given these results in lab, we hypothesized that HEX may contribute to the psychotherapeutic process in treatment of post-traumatic stress-disorder. In a randomly-assigned double-blind clinical study, we diffused either HEX or control (blinded as A & B) into the clinic during therapy. Analysis of the initial 10 patients implies a significant difference in clinical outcome, but we will not know which is HEX until planned unblinding at n=40.

226 **A Sensory Circuit For Social Learning**

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In social contexts, mice can learn about the safety of food through an association formed between food odors and the semiochemicals present in the breath or feces of other mice. This behavior is known as the social transmission of food preference and is mediated through the necklace olfactory subsystem via the Guanylyl Cyclase D (GCD) olfactory receptors (Munger et al., 2010). However, it remains unclear how the sensory information encoded by the GCD neurons are transmitted to the rest of the brain and how the olfactory system supports this form of social learning. Through a combination of viral tracing and optogenetics, we have identified a circuit between the GCD projection neurons in the olfactory bulb and basal forebrain which is necessary and sufficient for this olfactory-mediated social learning. The connectivity of the GCD olfactory circuit with the basal forebrain suggests that this network is suited not only for processing social odors, but also for improving learning. Indeed, activation of GCD projection neurons (through odor ligands, optogenetics, or chemogenetics) activates neurons in the basal forebrain and evokes acetylcholine release as measured through fiber photometry or GRIN-based calcium imaging. Collectively, our data suggests that the necklace olfactory system is functionally connected to the cholinergic system that is important for learning and memory. In addition to promoting social learning of food preferences, chemogenetic or optogenetic activation of GCD neurons enhances memory formation during social recognition and novel object tasks and enables optimal spatial navigation in complex environments. We propose that this sensory circuit may have evolved to recruit attention to support learning in a variety of ethological conditions which require flexible behavior.

228 **Exploring The Role Of Pup Odors In Experience Dependent Maternal Behaviors.**

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Mother mice engage in maternal behaviors such as pup retrieval with high accuracy and low latency. Nulliparous mice typically display little retrieval behavior but can begin retrieving after extended periods of pup exposure, indicating an experience-dependent learning process. While the auditory system plays a major role, previous studies in mice have shown that this behavior is also dependent on a functional main olfactory system. For example, impaired olfactory sensory neurons and piriform cortex lesions both disrupt maternal behaviors suggesting that the main olfactory system is involved. Despite this, little is known regarding how pup odors to contribute to the acquisition of maternal behaviors. To begin exploring this question, we first used a pup exposure paradigm in which pup-naïve nulliparous mice are allowed to interact with pups in the absence of the mother for 2 hours per day. Mice were pup exposed for either one or four consecutive days. After this exposure these mice were tested in a pup retrieval task and their retrieval behavior was compared to that of both non-exposed females and mothers. Overall, we find that four days of exposure produced pup retrieval latencies and accuracies comparable to those of mothers, whereas naïve control mice exhibited longer latencies and increased retrieval errors. Mice with one day of exposure displayed increased retrieval behaviors compared to controls, but less than those in the four-day exposure group suggesting that the acquisition of maternal behaviors in nulliparous mice is dependent on the amount of time interacting with pups. Current work is focused on exploring whether pup odor alone can drive behavior changes and the role a functional main olfactory system plays in both the acquisition and expression of pup retrieval behaviors.

230 **Respiration Encodes Social Valence And Relative-Rank During Chemosensory-Guided Social Interactions**

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Social interactions in mice are guided by chemosensory cues that dynamically reshape respiration and internal state. Respiratory patterns are tightly coupled with olfactory sampling and limbic activity, providing a continuous physiological readout of internal states. However, whether respiration encodes socially relevant information such as valence and dominance status during natural social interactions remains unclear. We recorded respiration in freely interacting mice during resident–intruder encounters with positive (juvenile), negative (aggressive CD1), and cagemate conspecifics. Respiratory patterns differed across social contexts and decoded social valence and dominance rank using leave-one-out cross-validated logistic regression, indicating that respiration carries structured social information beyond arousal. This finding implicates limbic valence circuits in shaping respiratory patterns. Because the basolateral amygdala (BLA) plays an important role in encoding social valence

and functionally interacts with the mPFC to regulate approach and avoidance behaviors, we hypothesized that optogenetic activation of CaMKIIα–ChR2–expressing BLA terminals in the mPFC would modulate social investigation and respiration. In a within-subject design, terminal activation produced modest and variable effects on both behavior and respiratory rate across animals. To assess the contribution of olfactory input to positive social interaction, juvenile encounters were examined before and after chemical ablation (methimazole, 75 mg/kg) of the main olfactory epithelium (MOE). MOE ablation reduced juvenile investigation, consistent with the role of olfactory cues in social engagement. These findings establish a framework for examining how limbic circuits interact with internal-state signals during social behavior.

232 **Social Interaction Drives Interbrain Synchrony In Olfactory And Prefrontal Networks**

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Social interaction is fundamental to individual well-being and depends on information exchange, behavioral coordination, and shared cognitive states between individuals. This interaction exhibits coordinated neural activity, termed interbrain synchrony (IBS), which encodes socially relevant information. IBS is observed in the medial prefrontal cortex (mPFC), a key region for social cognition. Respiration-entrained olfactory oscillations organize mPFC activity, but their role in IBS is unknown. Here, we test if coordinated olfactory inputs during social interaction promote IBS via an olfactory–mPFC circuit. We simultaneously recorded local field potentials (LFPs) from the mPFC and OB in freely behaving mouse pairs (n=21 pairs). IBS (Pearson's correlation of LFP power) was observed in both mPFC and OB , with respiration also synchronizing during social interactions. To rule out that IBS is caused by common sensory stimuli, we ran four controls. First, IBS only existed in pairs engaged in social interaction, but not across mice that each interacted with a different mouse. Second, olfactory epithelium ablation by methimazole did not abolish IBS, indicating that odor stimuli are not required. Third, investigation of a novel object, despite eliciting similar exploration, did not induce IBS. Fourth, to assess whether sustained social engagement enhances IBS, we allowed mice to interact through small windows in adjacent cages. IBS increased over time and peaked within the first minute of interaction. Finally, synchronized optogenetic activation of interneurons in the mPFCs or OBs did not alter social interaction. These findings indicate that IBS emerges only during direct social interaction, is independent of external sensory stimuli, and is not driven by inhibitory neuronal activity in these regions.

234 **Experience-Dependent Changes In Pup Odor Responses In Anterior Piriform Cortex During The Onset Of Maternal Retrieval Behavior**

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Mother mice display a variety of behaviors that ensure the survival of their offspring. One such behavior is retrieving pups that move out of the nest. This behavior is experience-dependent: naïve, nulliparous female mice do not reliably engage in retrieval behaviors but become increasingly efficient with pup experience. Most retrieval studies have focused on pup ultrasonic vocalizations and maternal auditory system plasticity in facilitating this switch. While the auditory system clearly plays a crucial role, previous studies in mice have shown that pup retrieval behavior is also dependent on a functional main olfactory system. For example, impaired olfactory sensory neuron function or piriform cortex (APC) lesions significantly reduce the occurrence of maternal behaviors. Despite these studies, little is known about whether or how pup odor coding may be altered following the onset of retrieval behavior. Here, we used calcium imaging in freely moving mice to explore changes in APC neuronal activity while females (n=5) interacted with pups at three time points: pre-pregnancy, as a new mother (P1), and as an experienced mother (P5). We find that mean pup-evoked APC responses were significantly higher in naïve females compared to following maternal experience, suggesting that maternal experience alters APC response strength. Interestingly, our data also show APC responses habituate over trials when females are naïve, but do not following maternal experience. Further, trial-to-trial population response correlations to pup odors become stronger with experience, suggesting that pup-evoked responses may become more consistent over time. Our findings demonstrate that like auditory cortex, APC undergoes a period of experience-induced plasticity during the transition to maternal behavior.

236 **The Role Of Anterior Piriform Cortex In Social Recognition In Mice**

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Engagement in proper social behaviors requires individuals be able to detect signals provided by other conspecifics, differentiate the information, and then act accordingly. For rodents, detection of social signals occurs through both the main and accessory olfactory systems and both circuits show importance for engaging in proper social behaviors. Within the main olfactory system, the anterior piriform cortex is the main odor processing region and demonstrates responses to social signals. We hypothesize that the anterior piriform cortex is an integral component for ability to engage in social recognition. We utilized head-mounted miniscopes to record neural activity of freely moving mice during a three-phase social recognition paradigm. Within a three-chambered social arena, mice were given the ability to interact with a same-sex conspecific and an empty cylinder for 5 minutes followed by a 10-minute intertrial phase. Then the mice were allowed to interact with a novel and the familiar same-sex conspecific for 5 minutes. Mice demonstrated social recognition through more time spent with and stronger neural responses to novel compared to familiar conspecifics. Additionally, a principal component analysis of neural activity during investigations showed separation based on familiarity. Our data appears to indicate two things: A) anterior piriform cortex plays a role in social recognition and B)

familiarity may drive neural population responses and coding. The information encoded within anterior piriform cortex is likely then relayed to other social behavior relevant brain regions. Currently we are working to elucidate the mechanisms that enable social recognition within anterior piriform cortex, what information is then relayed, and how the information is relayed to other social behavior regions.

238 **Caste- And Age-Specific Plasticity In The Antennal Transcriptome Of *Harpegnathos Saltator***

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The Indian jumping ant, *Harpegnathos saltator*, exhibits reproductive plasticity in which workers who win at in-colony dueling can transition to long-lived, egg-laying gamergates in the absence of queen pheromone, increasing lifespan ~5-fold. Preliminary data suggests that chronologically older workers transition more slowly than younger workers and may do so incompletely (partial reprogramming); however, the effect of age of transition on olfaction has yet to be studied. To test whether gamergate transitions from older workers result in partial olfactory reprogramming, antennae were sampled from behaviorally validated workers (nurses and foragers) and gamergates across 1-, 4-, and 7-month age classes. 4-month-old gamergates transitioned from 1-month-old workers, while 7-month-old gamergates transitioned from 4-month-old workers. RNA was extracted using a TRIzol protocol and libraries were sequenced at the University of Florida's ICBR. Reads were processed using a standard RNA-seq pipeline in HiPerGator, and differential expression analyses were performed in R with DESeq2. Principal component analysis (PCA) of all genes separated gamergates from workers, with gamergates exhibiting clustering by age; PCA based on *Or* gene expression did not explain this variation. Further, only three *Ors* were differentially expressed (DE) (padj <0.05) between gamergates and workers. In contrast, cytochrome P450 gene expression restored caste and age clustering in a PCA, with 44 DEGs (padj <0.05) divided between workers and gamergates. Comparisons between older gamergates and workers yielded more DEGs (1261, padj <0.05) than younger comparisons (330, padj <0.05), suggesting that transitions may not become increasingly partial with age. Further, these results indicate vital non-*Or* mechanisms in olfactory plasticity.

240 **Odors Count Globally: The Number Of Conscious Odor Perceptions Differs Between 17 Locations On Five Continents**

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Although people around the world perceive odors in broadly similar ways; however, it remains unclear whether they are equally aware of those present in the ambient air. Previous research on odor awareness has predominantly relied on self-report measures. To address this, we conducted a large-scale, global study with the aim of developing a comprehensive, multilevel model that would explain the variability in the frequency of conscious odor perception across geographic regions. This model would incorporate both individual and location-related factors. The study involved specialized chemosensory laboratories from 17 countries worldwide and, for the first time at a global scale, employed a behavioral measure of odor awareness based on odor counting performed 24 hours after the testing session. Our results revealed that location accounted for 15.2% of the variability in odor counts, while individual participant characteristics explained an additional 6.1%. Self-assessed odor awareness significantly predicted the number of consciously perceived odors; however, age, gender, and chemosensory sensitivity were not associated with odor counts. We discuss our findings in the context of previous reports and identify factors that could potentially be incorporated in future investigations to more precisely determine the mechanisms underlying global differences in behavioral odor awareness.

242 **A Novel Approach To The Assessment Of Odor Awareness**

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Odor awareness is a metacognitive capacity associated with the perception of environmental odors and their significance in everyday life. Studying odor awareness might provide valuable insights into individuals' interactions with olfactory environments that cannot be reproduced in laboratory settings (Nováková & Vojtušová Mrzílková, 2016). Odor awareness is also associated with individuals' engagement in olfactory exploration and scent-related behaviors (Sorokowska et al., 2018). However, research on odor awareness, especially among children, remains scarce. Existing measures demonstrate good psychometric properties but rely heavily on advanced verbal, cognitive, and abstract reasoning skills, which limits their applicability in young children. To address this gap, we aimed to validate a new method for assessing odor awareness in children: the OAS-C (Odor Awareness Scale for Children). The proposed method consists of an open-ended task in which children spontaneously name odors encountered in everyday life. In our study, we invited 151 children aged 4–9 to complete the OAS-C alongside the Children's Olfactory Behavior in Everyday Life questionnaire (COBEL) (Ferdenzi et al., 2008) to assess convergent validity. Olfactory performance was measured using the U-Sniff odor identification test. Food neophobia was included to examine divergent validity, and verbal fluency was assessed due to its potential influence on odor identification and task performance. Our results suggested that OAS-C is a valid method for measuring odor awareness in preschool children. OAS-C relies on verbal fluency, however, controlling for it, the correlation with COBEL remains significant and moderate. Children mostly listed plants and food-related items as fragrant objects. No gender differences were observed.

244 **Rapidly-Adapting Lingual Mechanosensory Parvalbumin+ Neurons Have Discrete Fungiform Receptive Fields But Show Evidence Of Convergence With Gustatory Neurons In The Nucleus Tractus Solitarius**

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In the trigeminal ganglion, we found that neurons expressing parvalbumin (PvalB) innervate one fungiform papilla, are low threshold rapidly adapting (RA) to mechanical force, responsive to brush stimulation, heavily myelinated, and are defined as A-fast by their conduction velocities. The rostral central (RC) subdivision of nucleus tractus solitarius (NTS) is where P2X2 expressing gustatory nerve fibers terminate. The RC subdivision of the NTS is weakly myelinated and PvalB labeling is sparse. In contrast, the rostral lateral subdivision of the NTS is heavily myelinated, PvalB labeling is robust, and continues through the laterally adjacent trigeminal nuclei. We have shown that the lateral border of the P2X2 terminal field demarcates the transition from gustatory to lingual mechanosensory. Here, we investigated whether gustatory neurons receive mechanosensory input from genetically identified PvalB neurons innervating the tongue, and whether optogenetic stimulation lingual PvalB+ neurons modulated taste responses in the NTS. Consistent with our trigeminal ganglion findings, PvalB+ neurons outside the P2X2 field were RA and A-fast. Low jitter (SD of the latency) indicated they were monosynaptic. Pvalb- neurons were slowly adapting (SA) or RA, and ranged from C to A-fast with monosynaptic or polysynaptic jitter. Gustatory neurons with lingual PvalB+ input were brush sensitive, defined as RA and A-slow, and had high jitter, suggesting polysynaptic circuitry. In contrast, Pvalb- gustatory neurons that were insensitive to brush were defined as SA or RA C-fibers, whereas PvalB- gustatory neurons that were sensitive to brush were also defined as SA or RA and ranged from C to A-fast. In a few cases, optogenetic stimulation of PvalB+ neurons innervating the tongue inhibited gustatory activity.

246 **Visualizing The Central Targets Of Peripheral Gustatory And Interoceptive Neurons By Transsynaptic Labeling**

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Peripheral sensory neurons of the trigeminal, gustatory and vagal ganglia relay information from chemical and mechanical stimuli to 2nd order neurons in the brainstem and spinal cord. Yet, identifying the specific target neurons of particular peripheral axon types is challenging. We produced a construct of wheat germ agglutinin (WGA) fused to mCherry for Cre-dependent monosynaptic anterograde tracing. We delivered *flex*.WGA/mCherry (mWmC) packaged in AAV-PHP.S into *Pirt*-Cre mice (in which all peripheral sensory neurons are Cre+). We detected mWmC as discrete puncta in the somata of neurons in the Nucleus of Solitary Tract (NST), Paratrigeminal Nucleus (Pa5) and Area Postrema (AP) in 11 mice. Fluorescence intensity in these 2nd order sensory neurons was significantly higher than in neurons in adjacent areas ($p < 0.0001$; Mann-Whitney 2-tailed unpaired t-test; 2300 neurons from 4 mice). Signal specificity was confirmed by injecting the above AAV into *Phox2b*-Cre (only gustatory and nodose peripheral neurons are Cre+) mice. Here, signal was lost from target areas of trigeminal and jugular axons. To enhance the transsynaptic signal, we produced AAV-PHP.S with mCherry replaced by mScarlet, a brighter protein with lower pKa (to promote stability in postsynaptic lysosomes). Fluorescent puncta in 2nd order sensory neurons were larger and more numerous in mice injected with mWmSc compared to mWmC, and intensity was significantly greater for mWmSc ($p < 0.0001$; Mann-Whitney 2-tailed unpaired t-test; 423 neurons from 4 mice). This trans-synaptic labeling system is now optimized to mark 2nd order neurons that are the targets of molecularly defined peripheral sensory neurons for gustation and interoception.

248 **Connectomic Mapping Of Pharyngeal And Gut Sensory Circuits In Adult *Drosophila***

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Feeding is regulated by both external sensory signals, such as taste, and internal sensory signals originating from the pharynx and gut. The recent completion of the Full Adult Fly Brain (FAFB) connectome presents an exciting opportunity to map these sensory inputs and their downstream circuits. While the external gustatory receptor neurons (GRNs) have been relatively well characterized, the internal pharyngeal and gut sensory neurons remain less understood. Here, we systemically identify their axonal projections in the FAFB connectome and examine their downstream circuits. We find that the stomodeal nerve, which carries afferent signals from the gastrointestinal tract to the brain, contains multiple types of sensory axons with distinct morphology and downstream connectivity. In addition, we identify sensory axons derived from different pharyngeal sense organs and find that chemosensory and mechanosensory neurons project to distinct regions of the subesophageal zone. Characterization of the second- and third-order neurons reveals the brain regions that receive inputs from pharyngeal and gut sensory neurons. Interestingly, a subset of these internal sensory neurons forms monosynaptic connections with various motor neurons and endocrine cells, suggesting that internal signals from the gut and pharynx may directly drive feeding-related motor programs and endocrine functions. Together, this study provides a foundation for further analysis of feeding-related internal sensory circuits and may offer insights into how external and internal sensory signals are integrated to regulate feeding behavior.

250 **Odor-Evoked Activity Outside Canonical Areas Of Olfactory Information Transmission Is Mapped By Fostrap And Downregulated By Diet-Induced Obesitydriven Changes In Metabolism**

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The homeostatic pathways that are activated by odors to influence metabolic state and motivational aspects of feeding are incompletely known.We utilized Fos2A-iCreER mice (TRAP2) to permanently tag odor-evoked neuronal ensembles across the olfactory system, hypothalamus, and midbrain in both control fed (CF) and moderately-high fat fed (MHF) animals. We selected the odor isopropyl tiglate (IPT) because its preferred ligand (Olfr160) has previously been shown to be vulnerable to diet-induced obesity. Compared to vehicle [mineral oil] groups, IPT exposure resulted in differential TRAP labelling in the glomerular, mitral, and granule cell layer of the olfactory bulb ($p < 0.001$); which extended to the anterior olfactory nucleus, piriform cortex, and cortical amygdala ($p < 0.05$). In contrast, the paraventricular thalamus and preoptic area had no measurable changes in TRAP activity, reflecting specificity of the odor and also internal energy state of the animal. Interestingly, IPT robustly activated feeding-related nuclei in the hypothalamus, including the arcuate (ARC), dorsomedial (DMH), and lateral hypothalamus (LH) ($p < 0.001$), while no change in TRAP activity was observed in stress sensing domains like the ventromedial hypothalamic nucleus and the suprachiasmatic nucleus ($p > 0.05$). Mice maintained on MHF diet exhibited a selective loss of odor-evoked ARC activity compared with CF animals ($p < 0.0001$), whereas DMH and LH TRAP activity was unaffected ($p > 0.05$). While IPT activated the nucleus accumbens (NAc) and medial septum (MS) neurons in CF mice ($p < 0.01$), it failed to do so in MHF animals ($p > 0.05$). Our study identified key brain regions linking chemosensation and metabolic state, and demonstrated an alteration in neural activity in hypothalamic areas upon obesogenic diet intervention.

252 **Learning Engages Medial Prefrontal Cortex Input To The Olfactory System**

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Learning transforms neural representations of odors such that the same odor is perceived differently before versus after learning. While many olfactory regions and cell types exhibit learning-dependent changes in odor representations, the origin of the signals that drive these changes remains unresolved. Across sensory systems, the medial prefrontal cortex (mPFC) plays a central role in learning and executive control. Using AAV-based anatomical tracing, our laboratory previously identified the tubular striatum (TuS, also known as the olfactory tubercle) as a privileged recipient of mPFC output amongst all other olfactory cortices, receiving convergent input from the prelimbic, infralimbic, and orbitofrontal cortices. Additionally, the TuS receives dense dopaminergic input from the ventral tegmental area, a neuromodulatory system critical for synaptic plasticity and learning. We then hypothesized that learning recruits the mPFC→TuS pathway and that this recruitment is influenced by dopamine (DA). To test this hypothesis, we recorded changes in calcium activity from mPFC→TuS projection neurons using fiber photometry with GCaMP8f while mice performed a two-alternative forced-choice odor discrimination task. Early in learning, odor-evoked responses in the mPFC→TuS pathway were weak. In contrast, after learning, odor-evoked responses were robust and reliable. Preliminary recordings of DA dynamics in the TuS using GRAB-DA1h from separate mice performing the same task revealed large odor-evoked DA responses during early learning, and ongoing work is examining how DA signaling evolves with experience. Together, these findings support a role for prefrontal cortex input to the olfactory system in odor learning and suggest that DAergic signaling shapes learning-dependent engagement within this circuit.

254 ***Anatomical And Molecular Organization Of Rnts Neurons And Their Metabolic Regulation***

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Taste perception is a major determinant of food intake, and it is dynamically modulated by hunger and satiety signals across species. In mammals, the anatomical and molecular organization of peripheral taste receptor cells and their cortical representation are well characterized. However, far less is known about how metabolic state shapes taste processing in subcortical brain regions such as the brainstem. To address this gap in knowledge, we investigate the anatomical organization of the rostral nucleus of the solitary tract (rNTS), the primary brainstem region that integrates and relays peripheral taste signals and examine how food deprivation modulates gene expression profiles in rNTS neurons. To accomplish this, we have performed RNAscope-based *in situ* hybridization, bulk nuclear RNA sequencing (RNAseq), and circuit mapping of molecularly defined subsets of rNTS neurons focusing on the excitatory ($VGLUT2^+$) and inhibitory ($VGAT^+$) subsets. We first mapped the projections of these neurons using anterograde and retrograde viral tracing, and then isolated rNTS-specific neuronal nuclei for RNAseq from mice under ad libitum–fed or 24-hour–starved conditions. Our preliminary analyses reveal distinct projection patterns and metabolic-state–dependent changes in gene expression within the rNTS. Together, these experiments aim to uncover molecular and anatomical profiles of excitatory and inhibitory rNTS neurons, including distinct adaptations within specific taste-sensing populations in response to food deprivation. By integrating genomics, neural tracing and functional imaging, we seek to unravel the molecular, anatomical, and physiological heterogeneity of rNTS taste circuits and elucidate their dynamic roles in regulating homeostatic feeding behaviors.

256 **Mapping Fos-Immunoreactive Neurons Activated By Intra-Oral Infusion Of Quinine, Sucrose Or Water Throughout The Brain Of B6 Mice**

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Fos immunohistochemistry was used to identify neurons throughout the B6 mouse brain activated by intra-oral (IO) infusion of 3.0 mM quinine hydrochloride (Q), 1.0 M sucrose (S) or filtered water (W). Fos-immunoreactive (Fos-IR) neurons were found in each nucleus and subarea examined following each treatment with a few differences in the number of labeled neurons among treatments. Specifically, IO infusion of Q and S elicited more Fos-IR neurons than W in the central medial (CM) and dorsomedial (DM) subareas of the parabrachial nucleus (PBN) and the central medial (CeM) amygdala (ps<0.05). Infusion of Q led to more Fos-IR neurons than W in the central lateral (CL) PBN and the parvocellular reticular formation (PCRT, ps<0.05). The only area where IO infusion of Q and S elicited a different number of Fos-IR neurons was the PCRT which responded more to Q (p<0.05). Therefore, IO infusion of Q and S did not activate a different number of neurons in almost all taste-related brain areas. However, a cluster analysis of the number of Fos-IR neurons in all 29 nuclei and subareas examined revealed that populations of neurons distributed among these brain regions respond best to Q, S or both Q and S. Specifically, the Q-best cluster tended to include more posterior structures like the nucleus of the solitary tract, RT and most of the PBN. The S-best cluster included more anterior structures like the bed nucleus of the stria terminalis, nucleus accumbens and orbitofrontal cortex. And, the cluster of areas that responded better to Q and S than W included the amygdala, gustatory and piriform cortices and a few PBN subareas. Therefore, the data suggest that collections of neurons among taste-responsive brain areas are important for distinguishing Q and S from water as well as identifying the specific tastant.

258 **Organization Of Central Nucleus Of The Amygdala Neurons That Project To The Caudal Nucleus Of The Solitary Tract, Rostral Nucleus Of The Solitary Tract, And Parabrachial Nucleus.**

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The nucleus of the solitary tract (NST) and parabrachial nucleus (PBN) are the first and second central synapses for ascending gustatory signals from the oral cavity and visceral signals from the gastrointestinal tract. Moreover, spatially separate regions of the NST are associated with these distinct sensory inputs, with the caudal NST (cNST) processing visceral information and the rostral NST (rNST) gustatory information. We have previously shown that neurons in the central nucleus of the amygdala (CeA) that project to the rNST and PBN are largely distinct populations. The present experiments tested the premise that CeA projections to the cNST also arise from a subpopulation of neurons distinct from those projecting to rNST or PBN. In C57 wild-type mice, we injected different retrograde tracers into the cNST and rNST or into the cNST and PBN. Following paired cNST/rNST injections, we counted a total of 1,864 retrogradely labeled CeA neurons with 661 positive for both fluorescent markers, considered dual target neurons (35.4%). For paired cNST/PBN injections, 122 out of 991 retrograde labeled CeA neurons contained both markers (12.3%). Together with our previous results, the present observations suggest that the CeA is organized into large subpopulations of intermingled neurons that target distinct brainstem nuclei. Given that CeA neurons are GABAergic, this could allow for activation of a specific CeA-brainstem pathway by extrinsic inputs and simultaneous inhibition of other CeA-brainstem pathways by intrinsic inhibitory connectivity.

260 **Neural Control Of Tongue Blood Flow By Brainstem Parasympathetic Circuits During Orofacial Behaviors**

Jun Takatoh, Bin Chen, Aya Miyazaki
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Eating demands intense and sustained tongue activity, necessitating coordination between motor output and vascular regulation. Unlike most skeletal muscles, whose blood flow is regulated primarily by sympathetic autonomic inputs during exercise, the tongue receives dual sympathetic and parasympathetic innervation, suggesting distinct mechanisms of blood flow regulation. How these mechanisms operate during parasympathetic-dominant eating behavior remains poorly understood. Using cell-type-specific viral tracing in mice, we identified a parasympathetic circuit originating in the superior salivatory nucleus (SSN), a parasympathetic brainstem nucleus, that forms monosynaptic projections to tongue-resident parasympathetic neurons (intralingual parasympathetic neurons, ILPNs) innervating the tongue vasculature. Immediate early gene expression analysis showed that both SSN neurons and ILPNs are recruited during licking, consistent with engagement of this circuit during oral motor function. To assess functional relevance, we combined circuit-specific chemogenetic manipulation with laser speckle imaging of the tongue in anesthetized animals and found that selective activation of SSN neurons robustly increases tongue blood flow. In behaving, head-restrained animals, activation of this pathway increased licking amplitude, linking parasympathetic circuit activity to vascular and motor aspects of oral behavior. Together, these results identify a brainstem parasympathetic circuit that regulates tongue blood flow during orofacial behavior and suggest that intralingual parasympathetic neurons (ILPNs) serve as a tongue-resident interface through which central autonomic activity coordinates local vascular physiology with oral motor behavior.

262 **Chemogenetic Activation Of Amygdalar Prodynorphin Neurons Modulates Taste-Guided Licking Behavior In Mice**

Jinrong Li, Christian Lemon
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The central nucleus of the amygdala (CeA) is a critical hub for processing the hedonic value (appetitive & aversive) of tastes. Recent work identified a population of prodynorphin-expressing (Pdyn+) neurons in this area that selectively encodes sweet attraction, yet their role in orosensory preferences for taste is unknown. Here we investigated how chemogenetic activation of CeA Pdyn+ neurons affected mouse taste-guided licking behavior in brief-access fluid exposure tests, which capture oral sensory/tongue control of licking behavior. Intracranial delivery of Cre-dependent viruses in female and male *Pdyn_Cre* mice induced expression of the excitatory designer receptor hM3Dq:mCherry (hM3Dq mice, n = 13) or fluorophore mCherry alone (mCherry control mice, n = 8) in CeA Pdyn+ neurons. Several weeks later, hM3Dq and mCherry mice entered brief-access tests where they could lick solutions during discrete, seconds-long trials. Stimuli included concentration series of the behaviorally appetitive sugar sucrose (0, 0.1, 0.3, 0.5, 1 M) and the innately avoided bitter taste stimulus quinine (0, 0.1, 0.3, 1 mM). A blinded experimenter administered intraperitoneal injection of saline before daily sucrose tests for 4 days followed by daily injection of the hM3Dq ligand deschloroclozapine (DCZ, 0.1 mg/kg) before sucrose tests 4 days in both hM3Dq and mCherry mice. With DCZ, hM3Dq mice displayed greater average licking of sucrose (i.e., enhanced appetitive responding) with concentrations lower than 0.5 M, in comparison to mCherry mice and to saline injection in hM3Dq mice (group x sucrose x injection interaction, $F(4,68) = 2.7$, $p = 0.035$). Quinine analyses are on-going. Current available data suggest that CeA Pdyn+ neurons participate in appetitive taste-guided licking behaviors. Support: NIH DC011579

264 **Central Nucleus Of The Amygdala Neurons That Project To The Nucleus Of The Solitary Tract Are Influenced By Input From The Parabrachial Nucleus**

Sean Masterson, Abigail Muccilli, Robert Lundy
University of Louisville School of Medicine, Louisville, KY, United States

The central nucleus of the amygdala (CeA) is a major source of descending input to the gustatory regions of the parabrachial nucleus (PBN) and rostral nucleus of the solitary tract (rNST) and can modulate neural processing of taste information. Moreover, CeA-to-PBN and CeA-to-rNST neurons are intermingled but largely distinct populations. However, the origin of inputs to these subpopulations of CeA neurons remains unknown. We do know that PBN projects heavily to the CeA and could be one source of input that engages CeA-to-brainstem projection neurons. To test this premise, we injected an AAV virus into the PBN to anterogradely infect axon terminals in the CeA with the excitatory opsin ChR2(H134R) and the green fluorescent protein EYFP. In the same animal, cholera toxin b subunit conjugated to a red fluorescent protein (CTb-568) was injected into the ipsilateral rNST to retrogradely label CeA-to-rNST neurons. Following two-weeks for transport and gene expression, brain slices containing the CeA were prepared for whole-cell patch clamp recording from CTB-568 positive neurons combined with blue light activation of ChR2 axon terminals. Our results show that photoactivation of ChR2 produced excitatory postsynaptic potentials (EPSPs) in most CeA-to-rNST neurons (30 out of 34). In 4 of these responsive neurons, the EPSPs were followed by inhibitory postsynaptic potentials that were blocked by bath application of the GABA receptor antagonist bicuculline. Together with a recent study from my lab showing that the PBN is a major target of rNST neurons receiving CeA input, this organization could represent a brainstem-amygdala circuit whereby ascending gustatory signals can activate inhibitory CeA feedback to rNST that in turn adjusts excitatory input from PBN to CeA.

266 **Remembering Odors In Order**

Theresa L. White[1], William Fredborg[2], Caitlin M. Cunningham[1], Jonas K. Olofsson[2]
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How do people remember a series of odorants? Although a good deal is known about the way that human working memory (WM) handles verbal, visual and spatial stimuli when presented in a series, very little is known about how olfactory stimuli may engage WM capacities. The present study asked whether olfactory working memory (OWM) performs similarly to well-established WM findings in other stimulus domains in terms of (1) serial position (primacy and recency), (2) transposition errors and (3) grouping effects. The experiment involved odor stimulation using an olfactometer, instructions and sniff-cues presented on a computer screen, and button-press responses on a keyboard. Participants smelled four odorants in a sequence, followed by a probe odorant. Participants responded to the probe by determining the serial position in which it had been presented. Each person experienced some lists that were temporally uniform, as well as those that had a longer pause between the second and third odorant, allowing the possibility of a grouping effect. We found a recency effect, but no primacy effect in serial position, and transposition errors such that serial positions adjacent to the target were over-represented. No effect of temporal grouping was observed, either due to manipulation being insufficient or the uniqueness of olfactory memory. These results indicate that OWM shares similarities with verbal, visual, and spatial WM, but more research is needed before domain-general theoretical frameworks for human WM can be established.

268 **A Method To Measure Restored Odor Perception In Non-Human Primates**

Tatsu Kobayakawa[1], Hidekazu Kaneko[1], Aya Takemura[1], Yasuko Sugase[1], Masayoshi Kobayashi[2], Eisuki Ishigami[2], Daniel Coelho[3], Richard Costanzo[3]
[1]National Institute of Advanced Industrial Science and Technology, Human Informatics and Interaction Research Institute, Tsukuba, Japan, [2]Department of Otorhinolaryngology-Head and Neck Surgery, Mie University Graduate School of Medicine, Mie, Japan, Tsu, Japan, [3]Department of Otolaryngology-Head and Neck Surgery, Virginia Commonwealth University School of Medicine, Richmond, VA, United States

Recent studies suggest that electrical stimulation of the olfactory system may effectively evoke smell

perception. Before human application of an olfactory implant system, proof-of-concept functional validation in an animal model is essential. A critical requirement for such validation is a reliable method to assess odor perception in animals. The aim of this study was to establish a protocol for accurately determining odor perception in a non-human primate (NHP). Prior to the olfactory experiment, a monkey (*Macaca fuscata*) had been trained to fixate on a small target to obtain a reward. During the experiments, the monkey was seated in a primate chair with its head immobilized using a custom-fitted mask and positioned facing a monitor. Eye position was continuously monitored with an eye-tracking system. For the olfactory task, a fixation target appeared at the center of a screen. When the monkey maintained fixation for a predetermined duration, one of eight conditions (seven odorants or odorless air) was presented. Following each odor presentation, water was delivered as a reward; conversely, no reward was given after odorless trials. Because the specific odor qualities that might be elicited by electrode-based olfactory stimulation were unpredictable, the training paradigm focused on detecting the presence or absence of olfactory input rather than discriminating among odor qualities. To reinforce this, after the initial presentation of seven odors, each odor was subsequently mixed in equal proportions to alter odor quality during training. In conclusion, this protocol provides a reliable method for determining odor perception in NHPs using chemical stimulation and can serve as a foundation for future studies involving electrical stimulation of the olfactory system. This project was funded by SRT.

270 **Acute And Chronic Olfactory Epithelial Inflammation Differentially Impact The Olfactory Bulb, Hippocampus, And Cognitive Function**

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Olfactory epithelial (OE) inflammation disrupts the sense of smell and has been associated with cognitive dysfunction following viral infections such as COVID-19. Both acute and chronic inflammation damage olfactory sensory neurons in the OE, causing hyposmia/anosmia. However, the mechanism underlying olfactory epithelial inflammation-induced cognitive deficits is unknown. Using the methimazole-induced acute OE inflammation mouse model, we found that acute inflammation did not affect hippocampus-mediated spatial learning and memory function assessed by Barnes Maze test in both sexes. Although acute OE inflammation increased inflammatory cytokines, TNFα, IL-6 and IL-1β, as well as microglial activation and leukocyte infiltration, measured by CD68 and CD45, in the olfactory bulb of male mice, it did not induce inflammatory responses in the hippocampus of either sex. Using the inducible olfactory inflammation mouse model, we found that chronic OE inflammation reduced spatial learning and memory in both sexes. Chronic inflammation increased pro-inflammatory cytokines, microglial activation, and leukocyte infiltrations in the olfactory bulb of both sexes. Interestingly, 4 weeks after stopping chronic inflammation induction, when the OE is reconstituted and the smell function is restored, cognitive function was fully recovered in females but not in male mice, suggesting a sex difference in cognitive recovery following chronic OE inflammation-induced deficits. The hippocampal pathology during the chronic OE inflammation and recovery phases is under investigation. Together, these data suggest that acute and chronic OE inflammation differently affect cognitive function, and there might be an OE-OB-hippocampal inflammation pathway responsible for chronic OE inflammation-induced learning and memory deficits.

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

Kira Steinke[1], Emily Gibson[1], Diego Restrepo[2]
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In nature animals, such as rodents, routinely demonstrate the ability to collect, process, and integrate sensory information about the world to survive by being proficient in finding food, avoiding threats, and selecting mates. Importantly, the effectiveness of these behaviors is rooted in the interplay between olfaction and experience 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), as a key player in learning and memory. 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 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. The work presented here utilizes two-photon microscopy and halorhodopsin inhibition to investigate the behavioral relevance of these cells, particularly their expression of Calbindin2, and the effects of inhibition on these populations during the go/no-go task. Ultimately, these studies will help to elucidate the roles of Calbindin2 expressing cells during olfactory discrimination task, as well as further the field's knowledge on molecular aspects and expression patterns of DPTCs, helping to uncover crucial details about how memories are formed and retrieved in the brain.

274 **Dopaminergic Nuclei Track The Uncertainty Of Olfactory Sensory Information**

Sam H. Lyons, Pao Alicea-Roman, Ludwig Zhao, Jay A. Gottfried
University of Pennsylvania, Philadelphia, PA, United States

Natural odors are complex mixtures that flit about in space and time, changing in concentration and quality from one second to the next. Yet the human olfactory system is remarkably good at maintaining stable olfactory representations. How does this system remain robust to the noisy statistics of natural odors? We test a solution to

this question proposed by predictive coding. Under this scheme, reliable sensory information is amplified, and noisy sensory information is suppressed. Thus, the highest quality information is prioritized for further processing. This amplification and suppression scheme is thought to be mediated by neuromodulatory systems that amplify and suppress neural representations. To test this hypothesis, we developed a noisy odor-prediction paradigm under 7-Tesla fMRI, in which participants learned noisy cue-odor associations. By employing ultra-high-resolution fMRI, we were able to examine activity in tiny neuromodulatory nuclei during this task. Using computational modelling, we discovered that the uncertainty of odor information was tracked by the functional coupling between dopaminergic nuclei and a network associated with olfactory sensory information. The strength of this coupling then predicted task performance. These results are consistent with the role of neuromodulators in predictive coding and further suggest a mechanism for robust odor perception in natural environments.

276 **Online Integration Of Associatively Activated Odor Memories In The Human Brain**

Xiaolin Qiao, Lauren A. Wolters, Liam P. McMahon, Jared G. Newell, James D. Howard
Department of Psychology, Brandeis University, Waltham, MA, United States

Adaptive decision making requires both directly observable information and inferences made on past experience with other related stimuli and situations. One potential inference mechanism is known as online integration, in which latent representations are associatively linked to relevant stimuli prospectively, prior to the point of a later decision. Recent experiments in humans and non-human animals point to medial temporal lobe and ventral prefrontal cortex as key substrates supporting inference-based decision making. However, whether these regions specifically support online integration in humans is not known. We recently implemented a representation-mediated learning task (RML) in conjunction with fMRI (N=30) to test this hypothesis. In this task, participants first learned associations between visual symbols and two distinct appetitive food odors. We then acquired pleasantness ratings for symbols and odors before and after one of the symbols was paired with an aversive sound. Behaviorally, participants showed a selective decrease in the pleasantness rating for the odor previously paired with the aversively conditioned symbol. Using multivoxel pattern analysis, we first identified brain activity patterns reflecting expected odor identity from the appetitive learning phase in orbitofrontal cortex (OFC) and parahippocampal gyrus (PHG). Critically, we found that these odor identity expectations were reactivated in the OFC and PHG when the visual cue was presented during aversive conditioning. These preliminary findings provide a potential neural mechanism by which previously learned odor associations are prospectively linked to the aversive sound, despite the odors never being directly paired with the sound.

278 **Evaluating Behavioral Expression Of Neophobia Across A Spectrum Of Tastes**

Walter/J Krueger, John/D Boughter Jr., Max/L Fletcher
Department of Anatomy and Neurobiology, Integrated Biomedical Sciences Program, College of Graduate Health Sciences, University of Tennessee Health Science Center, Memphis, TN, United States

Taste neophobia is an established behavioral phenomenon in rodents and serves as a critical model for studying the intersection of learning, memory, and adaptive decision-making. Neophobia limits exposure to toxic substances by minimizing initial consumption until the safety of the novel food is established. Currently, the prevailing opinion is that neophobia is generalized to all novel tastants and that expression of neophobia is characterized by a decreased level of palatability. However, this conclusion is based almost exclusively on studies using saccharin. To date, no studies have directly compared the extent of neophobia to a variety of different tastes to fully test the above hypotheses. Here, we quantified the behavioral expression of neophobia in naïve mice to a wide range of novel tastants using a brief-access paradigm in which mice alternated licking of one of the stimuli and water for 5 days. For 2 concentrations of saccharin, mice displayed typical neophobia, with a robust increase in preferential licking of saccharin on days 2-5. We also found neophobic behavior in response to one concentration of QHCl, but not in response to sucrose, MSG, or NaCl. Therefore, neophobia was taste dependent, with only saccharin and quinine causing reduced initial intake followed by attenuation over days. A sucrose-quinine mixture produced neophobia similar to that elicited by saccharin, supporting the premise that the complex sweet-bitter taste of saccharin makes it an ideal neophobic stimulus. This has implications for understanding the natural organization of this behavior, with the notion that animals initially avoid novel appetitive foods that may contain a hint of toxicity (i.e., bitterness) but then increase consumption of those foods following the absence of negative post-ingestive consequences.

10:15 - 12:15 PM	Bird Key

LATERALIZED AND INTEGRATED PROCESSING IN THE OLFACTORY SYSTEM

Chair(s): Thorsten Kahnt and Clara Raithel

10:15 ***Lateralized And Integrated Processing In The Olfactory System***

Thorsten Kahnt
NIDA IRP, Baltimore, MD, United States

The olfactory system universally relies on sensory input from two anatomically distinct channels (e.g., antennae, nares, nostrils). For some tasks, these separate streams of information are best kept separate, whereas for others, perception and behavior benefits from their integration. This symposium will highlight recent advances in our understanding of how olfactory information from the two channels is processed in the brain, spanning a wide range of neuroscience methods (behavior, electrophysiology, imaging, computation) and model organisms (flies, rodents, humans). First, Naz Dikecligil will present data from intracranial recording experiments in humans, showing that bilateral odor stimulation evokes temporally segregated odor representations. Second, Clara Raithel will discuss human behavioral and neuroimaging data from experiments with single-nostril odor stimulation. Next, Venki Murthy will present electrophysiology evidence on how bilateral odor information is integrated in the rodent brain. Finally, Aravi Samuel will discuss calcium imaging data from larval Drosophila, revealing laterality from sensory neurons to mushroom body output neurons. Together, this symposium will provide a cross-species overview on how lateralized olfactory information is shared across hemispheres, and how it may be kept separate, to optimally inform behavior.

10:25 **Piriform Cortex Takes Sides: Temporally-Segregated Odor Representations From Ipsilateral And Contralateral Nostrils Within A Sniff**

G. Naz Dikecligil[1], Andrew I. Yang[2], Kathryn A. Davis[1], Jay A. Gottfried[1]
[1]University of Pennsylvania, Philadelphia, PA, United States, [2]Barrow Neurological Institute, Phoenix, AZ, United States

The human nose, often thought of as a singular sensory organ, contains two distinct sensory channels arising from the left and right olfactory epithelia. Although there has been extensive work on how the olfactory system responds to odorants, relatively little is known on how the olfactory system ultimately integrates odor information arising from its two segregated sensory channels. In this study, we set out to investigate whether the human piriform cortex (PC) maintains distinct and separable representations of odor information arising from each nostril. We recorded intracranial electroencephalogram (iEEG) signals from PC of epilepsy patients undergoing invasive monitoring, enabling us to characterize odor responses with high spatial and temporal resolution. Subjects participated in an odor identification task, where odors were delivered either to the left, right, or bilateral nostrils via a computer-controlled olfactometer. We analyzed the time course of odor identity coding and found that, on average, odor identity information from the ipsilateral nostril is encoded ~480-ms faster than the contralateral nostril. During bi-nostril odor sampling, odor information emerged in two temporally segregated epochs, with the first epoch corresponding to the ipsilateral and the second epoch corresponding to the contralateral odor representations. These findings reveal that PC maintains distinct representations of odor input from each nostril through temporal segregation, highlighting an olfactory coding scheme at the cortical level that can parse odor information across nostrils within the course of a single inhalation.

10:55 **Exploring Lateralized Processing In The Human Olfactory System**

Clara U Raithel, Jaylen Worthy, Rhianna Sullivan, Thorsten Kahnt
National Institute on Drug Abuse, Intramural Research Program, National Institutes of Health, Baltimore, MD, United States

The human olfactory system receives sensory information from two anatomically distinct nostrils. Existing evidence on how these separate streams of information are processed in the human brain and used for behavior is inconclusive. Furthermore, nasal cycling is often ignored in the existing literature or discussed purely as an afterthought. In this study, we ask how the olfactory system encodes sensory inputs from the left and right nostril, and how both behavior and neural representations are influenced by nasal cycle. For this purpose, we developed a novel olfactory perceptual decision-making task in which we deliver binary odor mixtures to the left or right nostril and ask participants to indicate the dominant component in the mixture. We simultaneously record brain activity using fMRI and measure nasal airflow in each nostril separately to account for differences in neural representations as a function of the nasal cycle. Our findings suggest that participants can successfully discriminate unilaterally delivered odor mixtures. Interestingly, although participants cannot reliably determine the site of odor stimulation (left vs. right nostril), brain responses in primary olfactory regions are highly lateralized, showing significantly stronger responses to ipsi- compared to contralateral odor delivery. This finding is broadly in line with the existing empirical evidence on primarily ipsilateral anatomical projections from the olfactory periphery to the primary olfactory cortex.

11:15 **Bilateral Integration Of Odor Information In The Mouse**

Venkatesh N Murthy[1,2], Leannah Schmitt[1,2], Siddharth Jayakumar[1,2], Julien Grimaud[3]
[1]Center for Brain Science, Harvard University, Cambridge, MA, United States, [2]Dept of Molecular & Cellular Biology, Harvard University, Cambridge, MA, United States, [3]SupBiotech, L'école des ingénieurs en biotechnologies, Paris, France

In the mammalian olfactory system, information from each nostril is thought to be mapped in a distributed and fragmented manner in higher brain regions, such that the same odor environment may be represented independently in the two sides. How can an animal create a consistent and unified internal representation from these differing pieces of evidence? The earliest brain region with interhemispheric projections is the anterior olfactory nucleus (AON), making it an excellent candidate for bilateral integration of odor information. We have found that the responses to odors sensed through the two different nostrils are highly correlated in each side of the brain. Such aligned representations mean that a population of cortical neurons will have very similar responses whether the animal smells the odor through one nostril or the other. With a simple mathematical model, we showed that random interhemispheric connectivity leads to uncorrelated representations, hence the mapping must be structured in some way. Indeed, matched odor representation can readily arise from conventional correlation-based, Hebbian synaptic plasticity of initially unstructured connections. Using viral tracing of specific subtypes of neurons within the AON, we have found that interhemispheric projections arise exclusively from glutamatergic neurons, but their axons target both glutamatergic and GABAergic neurons in the contralateral side. Optogenetics-assisted synaptic physiology revealed that contralaterally-projecting AON axons readily evoke monosynaptic excitation followed by polysynaptic inhibition. Collectively, our experiments point to structured integration of information in the two hemispheres in early olfactory cortical areas, setting the stage for future investigations into the origin of this structure and its function.

11:45 **Brain-Wide Representations Of Olfactory Navigational Behavior In C. Elegans**

Helena Casademunt, Aravinthan Samuel
Department of Physics, Harvard University, Cambridge, MA, United States

Olfactory navigation towards improved environments requires a dynamic interplay between an animal's brain activity and body movement. The small size of C. elegans permits multi-neuronal imaging of brain-wide activity in response to defined olfactory environments. Its undulatory body permits a reduction of navigational movement to stimulus-dependent transitions between forward, reverse, and turning motor states. Here, we use brain-wide tracking microscopy to monitor the circuit for olfactory navigation in crawling worms climbing spatial odor gradients and immobilized worms responding to temporal odor pulses. In both crawling and immobilized animals, we identify strongly-correlated brain-wide activity patterns from olfactory sensory neurons to interneurons to premotor neurons. The spatial pattern of activity correlations between specific neurons in the brain is jointly dependent on sensory and motor activity, but also directly dependent on whether the worm is actively crawling in a spatial gradient (where body movement is coupled to sensory perception) or whether the worm is immobilized and subjected to odor pulses. The temporal dynamics of transitions between forward/backward motor states is directly dependent on whether the animal is actively crawling or immobilized. Moreover, the temporal dynamics of neurons that underlie motor state transitions are modulated by crawling and immobilization. The brain-wide representation of olfactory response and decision-making are broadly reconfigured by an animal's body movements within its odor environment.

10:15 - 12:15 PM	Sawyer Key

NEW APPROACH METHODOLOGIES (NAMS) IN CHEMOSENSORY AND INTEROCEPTION RESEARCH

Chair(s): Ben Smith and Danielle Reed

10:15 **New Approach Methodologies (Nams) In Chemosensory And Interoception Research**

Benjamin Smith, Danielle Reed
Monell Chemical Senses Center, Philadelphia , PA, United States

Chemosensory and interoceptive systems represent a primary interface between the external chemical environment and internal physiology, positioning them at the center of “exposome” science. This symposium examines the role of New Approach Methodologies, emphasizing their integration into established experimental traditions rather than their use in isolation. From a regulatory and exposure science perspective informed by work across academia, industry, and government, the session highlights how human-relevant NAM platforms, including organoids, *ex vivo* transitional systems, and computational models, can strengthen links between exposure, dose, and biological response. Speakers will underscore the continued importance of experimental systems that preserve intact neural circuits, sensory-driven behavior, and learning, which have been central to foundational discoveries in chemosensory neuroscience, including work that has defined how the brain reads olfactory, gustatory, and interoceptive signals. By drawing on complementary examples across model systems, the symposium emphasizes convergence and cross-validation as essential scientific principles. Discussions will focus on how insights from animal studies inform the design and interpretation of NAMs, and how NAMs in turn can refine hypotheses. Framed within an exposome context, this session aims to foster inclusive and rigorous dialogue across the AChemS community on how best to integrate emerging and established approaches to advance chemosensory science.

10:25 **Building Confidence In Nams: Lessons From Regulatory Science**

Thomas Hartung
Johns Hopkins University

10:55 **New Approach Methodologies In Olfactory Dysfunction: Human Organoids As A Species-Specific *In Vitro* Model**

Jennifer E. Douglas[1,2], Ankit Chauhan[1], Kang-Hoon Kim[2], Danielle R. Reed[2], Noam A. Cohen[1,2,3], Peihua Jiang[2], Hong Wang[2]

[1]University of Pennsylvania, Department of Otorhinolaryngology - Head & Neck Surgery, Philadelphia, PA, United States, [2]Monell Chemical Senses Center, Philadelphia, PA, United States, [3]Philadelphia Veterans Affairs Medical Center Surgical Services, Philadelphia, PA, United States

Olfactory dysfunction (OD) is common and has implications for safety, quality of life, and nutrition. Mouse models have been foundational in the study of OD; however, differences between mouse and human olfactory epithelium (OE) limit the translatability of results. Recent NIH guidance encourages a shift from animal to human-specific models in research, and organoids represent a New Approach Methodology (NAM) that can support this progress. We have developed a human olfactory organoid model using superior turbinate biopsies (which are positive for olfactory genes and proteins, indicating the presence of OE). Dissociated cells generate olfactory organoids when cultured in supplemented media, and the resulting organoids express key OE genes and proteins. They also contain cells with the characteristic appearance of olfactory sensory neurons (OSNs), which are responsible for transducing chemical information to the brain. As a control, organoids cultured from non-OE tissue do not express these markers. The olfactory organoids also show activation in response to select odorants, a surrogate of OSN function. Next, it will be important to determine whether cultures respond to the same complement of odorants as the human nose. It will also be crucial to mimic the OE microenvironment by co-culturing the organoids with immune cells. Drawing on our expertise in the diverse chemical structures of odorants, we plan to assess class-specific odorant response to better understand how well this model represents human olfaction. This human olfactory organoid NAM represents a promising step forward in the study of human olfaction and can be optimized for downstream studies to provide insight for diagnostic and therapeutic purposes.

11:15 **Chicken Egg As A Translational New Approach Methodology (Nam) In Sensory Science: Insights From Genotoxicity Studies**

Tetyana Cheairs
Department of Pathology, Microbiology and Immunology, New York Medical College, Valhalla, NY, United States

Avian egg-based (*in ovo*) models, particularly those utilizing chicken embryos, have a long history of use in biomedical research, notably in cancer biology and immunology fields. The avian embryo is a metabolically competent, intact organism, with developmental and phenotypic similarities to mammals, offering advantages over invertebrate models. The Chicken Egg Model (CEM), was developed as a New Approach Methodology (NAM) to support or potentially replace short-term in vivo genotoxicity assays, serving as a follow-up screening test for compounds positive in regulatory in vitro tests. CEM uses embryo-fetal livers from White Leghorn chicken (*Gallus gallus*) eggs to assess chemical-induced DNA damage, such as the formation of nuclear DNA adducts and strand breaks. The model has been evaluated with diverse carcinogenic and non-carcinogenic chemicals, including flavor and fragrance materials, and has demonstrated robust performance for genotoxicity assessment. CEM can detect genotoxic potential of a broader range of compounds compared to in vitro assays

with S9 supplementation as evident from the concordance analysis of 87 chemicals. It revealed stronger correlation of CEM with in vivo genotoxicity assays (76% sensitivity and 79% specificity) than with in vitro assays (58% sensitivity and 45% specificity). In contrast to standard in vitro assays, CEM enables evaluation of other endpoints, including histopathology and tissue-specific gene expression. Moreover, physiological and behavioral responses of chickens to transient receptor potential (cTRP) and type 2 taste receptor (cT2R) ligands demonstrate functional chemosensory sensitivity. Collectively, these findings support CEM as a potential translational NAM in sensory science, particularly for the safety evaluation of sensory-active compounds.

11:45

Can Ai Understand The Physical World Without Smelling It? A Multimodal Representational Framework For Olfaction

Kordel France[1], Tian Yu[2], Michelle Niedziela[3]

[1]University of Texas at Dallas, Dallas, TX, United States, [2]Amai Consulting, LLC, Denver, CO, United States, [3]Nerdoscientist, LLC, Chalfont, PA, United States

Modern generative AI has achieved remarkable success in simulating human-like text and images. However, these models remain "disembodied," lacking the chemical grounding that is fundamental to biological intelligence. While AI integrates vision and audition to move closer to a "world model," the chemical senses, olfaction and gustation, remain largely absent. Consequently, AI lacks a true representation of the physical environment, relying on linguistic descriptions of smells rather than the underlying chemical reality.

We present a novel multimodal framework that integrates olfactory signals at the molecular level into a shared "joint-embedding" space alongside visual and linguistic data. Using public datasets, we developed a system where molecular structures, physical objects, and semantic descriptors are mapped into a unified multidimensional map. These results demonstrate the feasibility of this cross-modal alignment and serve as a "call to action": high-fidelity, curated chemosensory datasets are essential to unlock the full predictive potential of these models to bridge the gap between chemical structure and human perception.

By placing chemical senses on equal footing with vision and language, we move beyond building "smarter" AI, and invite the chemosensory community to lead the evolution of next-generation AI where the digitization of smell and taste fundamentally transforms how we interact with technology, our environment, and each other.

12:00 - 1:00 PM	Offsite
Outreach Event: St. Pete Beach Library	

12:15 - 1:30 PM	Lunch On Own
Lunch On Own	

1:30 - 2:30 PM	Bird Key
Business Meeting	

Get involved! All members are welcome and encouraged to attend.

2:30 - 3:30 PM	Bird Key
BOOST Lecture	

Chair(s): Arianna Maffei

2:30 **Introduction**

2:30 **Flight By Night, Or The Ecological And Anatomical Context Of Bat Chemosensory Evolution**
Liliana Dávalos
Professor, Department of Ecology and Evolution, Stony Brook University

3:45 - 5:45 PM	Pavilion
Poster Session IV	

201 **Olfactory Input Modulates Peripheral Trigeminal Responses During Mixed Stimulation.**

Keven Lapointe[1], Johannes Frasnelli[1,2,3]

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The trigeminal system, alongside smell and taste, constitutes a third chemosensory modality. It is responsible for sensations such as warmth, cooling, and tingling. The olfactory and trigeminal systems interact at multiple levels to modulate odor perception, from the nasal mucosa to central structures. More specifically, olfaction appears to amplify trigeminal perception, whereas trigeminal activation tends to reduce olfactory perception. However, the mechanisms underlying this interaction remain poorly characterized, particularly at the peripheral level. A better understanding could clarify alterations observed in olfactory disorders and advance our knowledge of human chemoperception. We used negative mucosal potentials (NMP) to record peripheral trigeminal activity with custom-made Ag/AgCl electrodes placed in the respiratory epithelium. Four experimental conditions were tested: pure olfactory (2-phenylethanol, PEA), pure trigeminal (CO_2), ipsilateral olfactory-trigeminal (PEA+CO_2 in the same nostril; IOT), and contralateral olfactory-trigeminal (PEA and CO_2 in opposite nostrils; COT). Repeated measures ANOVA revealed a significant effect of stimuli (Pillai's $V = .70$, $F_{2,7} = 8.13$, $p = .015$, $\eta^2_p = .70$). Bonferroni post-hoc comparisons indicated that the IOT condition elicited significantly higher amplitudes than CO_2 alone ($p = .023$) but not COT ($p = .108$), while the COT condition also did not produce higher amplitudes than CO_2 alone ($p = .105$). Together, these findings suggest that peripheral trigeminal responses are modulated by olfactory co-stimulation, highlighting a peripheral mechanism by which odor perception could also be shaped. In conclusion, this supports the existence of an early peripheral interaction preceding central integration between the olfactory and trigeminal systems.

203 **Stable By Design: What Ligand Binding Reveals About The Function Of Odorant-Binding Proteins In Mammals?**

Jérémie Topin[1], Maxence Lalis[1], Christine Belloir[2], Loïc Briand[2], Cornelia Meinert[1]

[1]Institut de Chimie de Nice, UMR CNRS 7272, Université Côte d'Azur, Nice, France, [2]Centre des Sciences du Goût et de l'Alimentation, CNRS, INRAE, Institut Agro, Université de Bourgogne, Dijon, France

Mammalian odorant-binding proteins (OBPs) belong to the lipocalin family and are widely expressed in the olfactory epithelium, where they are commonly associated with olfaction. However, despite the availability of high-resolution structures, their precise physiological role in olfaction remains poorly defined, and it is still

unclear whether OBPs are directly involved in odour recognition or rather play an ancillary role in odour processing. To investigate the molecular basis of ligand interaction with OBPs and its functional implications, we adopted an integrative approach combining molecular modelling, network analysis, site-directed mutagenesis, isothermal titration calorimetry (ITC), and synchrotron circular dichroism (CD) spectroscopy. We show that ligand entry occurs without inducing major conformational changes or destabilization of the protein, in both wild-type and mutant OBPs. Allosteric pathways modulate ligand access and affinity, yet the overall protein fold remains preserved throughout the binding process. This high stability argues against a direct role of OBPs in odor recognition, which typically relies on dynamic structural rearrangements. Instead, our results support a role for OBPs as robust scavenger or buffering proteins that capture, retain, and regulate the availability of odorant molecules[1]. Importantly, this intrinsic stability, combined with conserved ligand-entry mechanisms across the lipocalin family, makes OBPs particularly attractive as biological sensing elements for bio-nose applications, where durability, reproducibility, and sustained ligand binding are essential. [1]M. Lalis, et al. How Allosteric Mutations Control Ligand Binding in Lipocalin Protein: Odorant Binding Protein as a Test Case, *Cellular and Molecular Life Science*, 2025.

205 **Functional Specialization Of Respiratory And Olfactory Mucus Revealed By Proteomic Profiling**

Anna Kristina Hernandez[1,2,3], Karoline Lantzsch[1], Romain Topalian[4], Philipp Hubel[5], Katharina Schindowski[4], Jens Pfannstiel[5], Thomas Hummel[1]

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Introduction: Nasal mucus is essential for maintaining mucosal function and facilitating olfaction, yet it remains poorly characterized. Examining regional differences in its properties may provide insight into the physiologic mechanisms underlying nasal and olfactory function. This study analyzed the protein composition of nasal mucus to determine whether mucus from olfactory and respiratory mucosal regions shows distinct patterns of enrichment indicative of different underlying biological processes.
Materials and Methods: This cross-sectional study involved the collection of nasal mucus from 25 healthy adults (≥18 years) at two sites: the olfactory cleft (OC) and the medial surface of the inferior turbinate (respiratory mucosa, RM). Collection was done using cotton and viscose strips (Neurosorb, Vostra, DE) retained for 5 minutes. Proteins were analyzed using label-free quantitative proteomics (LFQ), in conjunction with 1D/2D Enrichment and PAN-GO Reactome Overrepresentation Analyses.
Results: A total of 6,156 proteins were identified. Welch's T-test with False Discovery Rate correction revealed 168 enriched proteins: 115 in the RM, 53 in the OC. RM enriched proteins were associated with immune functions, with the greatest enrichment observed for neutrophil aggregation and leukocyte migration (>100-fold). OC enriched proteins were predominantly associated with cilium organization and related structural processes.
Conclusion: RM mucus is associated with immune and inflammatory processes, reflecting its role in defense, while OC mucus is enriched in structural and metabolic proteins, likely contributing to epithelial maintenance. The distinct patterns of protein enrichment and biological processes indicate that mucus from these two nasal regions reflect very distinct physiologic contexts.

207 **Temporal Roles Of Olfactory Macrophages In Host Defense In The Olfactory Epithelium**

Brianna M Ramirez[1], Jiaying Liu[1], Hongwei Liu[1], Yunlu Sun[2], Yaejim Kim[1], Lark L Coffey[1], Qizhi Gong[1]

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The olfactory mucosa (OM) is uniquely vulnerable because olfactory sensory neurons remain directly exposed to the environment, increasing susceptibility to pathogens. Macrophages serve as critical first-line defenders by maintaining tissue homeostasis, surveying the local environment, and defending against pathogens. Although OM macrophages have been characterized, their responses to viral infection, particularly SARS-CoV-2 (CoV2), remain poorly understood. Here, we characterized OM macrophage diversity using single-cell RNA sequencing. In addition to phagocytic and antigen-presenting populations, we identified a novel macrophage subset marked by Cd163 and Mrc1 (CD206) expression. At homeostasis, macrophages localize to the basal layer and lamina propria. With CoV2 infection, macrophages infiltrated infected regions and upregulated inflammatory cytokines and antiviral genes by 2 days post-infection (DPI). By 6 DPI, infiltration extended beyond the initial infection site, with reduced antiviral gene expression and sustained upregulation of pathways associated with antigen presentation, neuronal remodeling, phagocytosis, and neurogenesis. During acute CoV2 infection, two monocyte populations were recruited to the OM. To determine whether infiltrating monocytes give rise to resident macrophages, we employed lineage tracing using CCR2-CreER; Rosa-LSL-tdTomato mice. With acute LPS exposure, monocyte infiltration was robust but returns to baseline by 8 weeks. During CoV2 infection, monocytic lineage cells did not contribute to the immediate macrophage population at 2 DPI; however, by 6 DPI, their presence was widespread throughout the OM. Together, these findings show that OM macrophages respond to CoV2 infection and suggest roles in host defense, tissue remodeling, and olfactory dysfunction.

209 **Ecological Roles Of Nasal Microbes**

Pia LaPorte[1], Jeba Chelladurai[2], Melissa Singletary[1,3]

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The nasal cavity microenvironment is home to diverse communities of bacteria playing critical roles in respiratory health and thought to play a role in olfactory function. Bacterial taxa in the nasal cavity have been shown to contribute to host immune responses, produce antimicrobial compounds, compete for resources, and maintain epithelial barrier integrity. Dysbiosis in this particularly vulnerable region is shown to disrupt protective functions and lead to overgrowth of opportunistic pathogens, the production of biofilms, tissue inflammation, and various diseases. To further evaluate the relationship between the bacterial community of the nasal cavity and its functional significance we aimed to characterize the regional microenvironments within the nasal cavity. Using a rat rodent model we isolated the ethmoidal labyrinth (E) and the olfactory (OE) and respiratory (RE) epithelial regions and performed shotgun metagenomic sequencing to a minimum of 165M Illumina reads (25Gbp) on the tissues. Preliminary analyses reveal statistically significant differences in alpha diversity between the two functional olfactory sensory regions of the Ethmoid and Olfactory Epithelium but not from the respiratory epithelium. Linear Discriminant Analysis however indicated several bacterial taxa that are uniquely isolated to each separate region. The ecological roles of these bacteria are being identified using the HUMAnN tools on the Galaxy platform to profile the presence or absence of microbial pathways from our metagenomic reads. An improved functional understanding of the nasal microbes will provide a valuable model for studying bacterial ecological processes and related implications on health and olfaction.

211 **Hunger States Drive Norepinephrine Concentration Dynamics In The Olfactory Epithelium**

Qiaohan Yang[1], Gregory Lane[1], Andrew Sheriff [1], Adam Dede[1], Naelly Arriaga[1], Seth Batten[1], Leonardo Barbosa[2], Paul Sands[2], Venkatesh Jatla[2], Jason White[2], Terry Lohrenz[2], Bruce Tan[3], P Read Montague[2], Christina Zelano[1]

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Internal state powerfully shapes sensory perception, likely through neuromodulators at the periphery, yet most descriptions of the olfactory system assume that odor signals pass from olfactory sensory neurons (OSNs) to the olfactory bulb (OB) largely unaltered. Despite this, the olfactory epithelium (OE) is densely innervated by sympathetic and parasympathetic nervous systems, and OSNs express receptors for diverse neuromodulators. However, state-dependent neuromodulation at this earliest stage remains largely unexplored. We address this gap with sub-second estimates of norepinephrine concentration changes from deep-learning-enhanced electrochemical recordings at the human OE to examine food odor-associated neuromodulatory changes across states of hunger and satiety. Participants completed a food-odor pleasantness task while hungry and again after eating to satiety. On each trial, participants sniffed food odors derived from their chosen meal or clean air, and rated pleasantness. Physiological signals (nasal airflow, ECG, EEG) were recorded concurrently. Preliminary data from five participants indicate that norepinephrine (NE) dynamics in the OE differ by internal state: during hunger, NE levels are sustained following food-odor sniffs and peak during inhalation, whereas during satiety, NE levels drop sharply during food-odor sampling. These findings suggest that autonomic neuromodulation at the OE tunes odor coding according to hunger state, revealing the peripheral olfactory system as an adaptive interface linking internal physiology to perception.

213 **Inflammation Is Necessary For Regeneration And Repair Of The Damaged Olfactory System Of Adult Zebrafish**

Lexus Putt, Olivia Wiley, Erika Calvo-Ochoa
Hope College, Holland, MI, United States

Zebrafish are an ideal model for studying injury-induced neural repair because they robustly regenerate neurons in both the central and peripheral nervous systems. Their olfactory system, composed of the olfactory bulb (OB) and olfactory epithelium (OE), is highly neurogenic and analogous to that of humans. In zebrafish, neuroinflammation supports regeneration after injury, in contrast to mammals. Rather than classic stellate astrocytes, the zebrafish brain contains radial glial–like astroglia and olfactory ensheathing cells that promote repair. Although inflammation is essential for brain regeneration, its role in OE repair remains poorly understood. We used a model of retrograde degeneration induced by excitotoxic OB lesions with quinolinic acid (QA) in adult zebrafish. Previous work showed that QA lesions cause OE neurodegeneration and olfactory deficits, followed by neurogenesis and functional recovery. Here, we examined inflammatory responses during early recovery at 1, 6, 24, and 72 hours post-lesion (hpl). Immunohistochemistry was used to assess inflammatory markers, including GFAP (glial fibrillary acidic protein; astroglial cells) and Lcp1 (lymphocyte cytosolic protein 1; leukocytes). To test the functional role of inflammation, we treated animals with the anti-inflammatory drug pranlukast, a cysteinyl leukotriene receptor antagonist.QA lesions increased leukocyte density in both the OB and OE; this response was reduced by pranlukast in the OB but not in the OE. Astroglial activity exhibited a bimodal pattern during acute recovery. Notably, anti-inflammatory treatment reduced cell proliferation in the OE. Together, these findings shed light on inflammatory processes following olfactory system injury and highlight their contribution to neural repair in adult vertebrates.

215 **Smell, Taste, And Flavor Perception In Parkinson&Rsquo;S Disease Compared To Non-Parkinsonian Olfactory Disorders.**

Shalini Balaji Vilvanathan[1], Majd Balbous[2], Maïné Dupuis Azizah[1], Nikolaus Arlt[1], Laurianne Thompson[1],

Johannes Frasnelli[1,3,4]
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Olfactory dysfunction is a common prodromal symptom of Parkinson's disease (PD), with previous studies suggesting a specific pattern. Identifying it can help in early detection and for improving disease management. Specifically, the retronasal component of olfaction could be a potential avenue for early detection. Odors reach the olfactory epithelium by two routes: orthonasal (while sniffing, by the nose) and retronasal (while eating/drinking, by the mouth). Retronasal olfaction is a major contributor to flavor perception, a multisensory modality that influences eating habits, food behaviours and nutritional health, Quality of Life (QoL) and is severely affected in PD. Our objective was to perform olfactory, taste and flavour functions, QoL assessment in three participant groups: (1) PD (27, age: 65.3 (8.9) years), (2) non-Parkinsonian olfactory dysfunction (NPOD) (29, age: 62.2 (7.9) years), and (3) age-matched healthy controls (HC) (32, age: 67.9 (8.0) years).
We observed significant group effects for orthonasal and retronasal olfactory threshold, discrimination, and identification, as well as flavor (all $p < .001$), but not for taste. The HC group consistently outperformed the other two groups across the various tasks. The NPOD group has a better awareness of the loss of smell and stronger effects on quality of life, when compared to PD. Further analyses may reveal intricate insights in flavor perception in PD. In conclusion, our study shows that smell, taste, and flavour perception are severely impaired in Parkinson's disease, while also revealing that patients are often unaware of the extent and adversity of the chemosensory deficits, in contrast to individuals with other olfactory disorders and age-matched controls.

217 **Impaired Olfactory Function In Substance Use Disorder**

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The sense of smell plays a key role in guiding motivated behavior, and olfactory function is impaired in clinical populations with dysfunctional approach-avoidance behavior, including major depressive and alcohol use disorder (AUD). Here, we tested olfaction in 40 individuals with substance use disorders (SUDs) other than AUD using the Sniffin' Sticks odor identification and olfactory threshold tests, versus 112 controls. Group differences were assessed with linear regression models, with diagnosis (SUD vs. controls) as a predictor, controlling for age, sex and smoking. Across a diverse range of substances used, individuals with SUDs had significantly lower *identification* scores than those in the control group. In contrast, olfactory *thresholds* did not differ significantly by diagnosis overall. However, exploratory analyses showed that men with SUDs had lower olfactory threshold scores (i.e., higher thresholds) than men in the control group, a difference that was absent in women. These results suggest that olfactory function is impaired in individuals with SUDs relative to controls. There are several plausible pathways by which differences in olfaction could be related to differences in hedonic processing, but longitudinal studies are needed to clarify the timing of olfactory impairment relative to substance use or SUD symptomatology.

219 **Long-Term Positive Effects Of Olfactory Training On Quality Of Life And Subjective Measures Of Olfactory Function**

Anja L. Winter[1], Pernilla Sahlstrand Johnson[2,3], Johan N. Lundström[1,4,5]
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Olfactory dysfunction after viral infection is a debilitating condition for which the primary recommended treatment is olfactory training, involving repeated, systematic exposure to odors over time. A new training tool using nasal inserts instead of hand-held devices has been developed to improve ease of use and adherence. In this randomized controlled trial (N = 111), we examined how olfactory training affects subjective olfactory function and quality of life, and whether outcomes differ between standard training and nasal-insert training in individuals with post-viral hyposmia. Participants completed an 8-week training program, with assessments before and after treatment and at 1-year follow-up. Overall, significant and sustained improvements were observed in both perceived olfactory function and quality of life. Critically, the nasal-insert group showed greater short-term gains in social functioning and quantitative olfactory performance, with enhanced olfactory benefits persisting at follow-up. Improvements in quality of life were correlated with subjective olfactory gains, particularly in the nasal-insert group. Findings from this trial provide insight into the benefits of olfactory training on subjective functioning and quality of life, as well as the efficacy of nasal insert training in post-viral hyposmia.

221 **Developmental And Task-Dependent Differences In Olfactory Perception In Autism: A Meta-Analysis**

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Background: Altered sensory processing are highly prevalent in autism spectrum disorder (ASD) and are now recognized as a diagnostic feature, appearing across all sensory domains. However, in comparison to other sensory areas, olfactory perception in ASD remains poorly characterized. Methods: We conducted a pre-registered meta-analysis to quantify differences in olfactory function between individuals with ASD and non-autistic controls (NAC) to identify methodological and demographic moderators. A comprehensive search of five databases identified 46 eligible studies, yielding 88 effect sizes from 1580 ASD individuals and 7706 NAC. Moderator analyses examined type of olfactory assessment, olfactory function tested, and age. Results: Overall, individuals with ASD showed significantly poorer olfactory performance than NAC (g = -0.38), with substantial heterogeneity observed across studies. Group differences emerged in psychophysical testing (g = -0.48) and informant reports (g = -0.53), but not in self-report or rating measures. Amongst olfactory functions tested, significant impairments were observed for psychophysically-measured odor identification (g = -0.53) and combined taste-smell measures from informant reports (g = -0.74). Children with ASD exhibited moderate deficits (g = -0.57), particularly in psychophysical identification (g = -0.80) and threshold (g = -0.65) tests, whereas no group differences emerged in adults. Conclusion: Olfactory alterations in ASD appear most pronounced in childhood and vary by assessment method and olfactory function measured. Our results highlight the need for age-appropriate standardized psychophysical measures to accurately evaluate sensory function in autism across the lifespan.

223 **Il-13 Impairs Olfactory Sensory Neurons And Induces Olfactory Dysfunction In A Human Olfactory Organoid Model**

Ankit Chauhan[1], Kang-Hoon Kim[2], Michael Xiang[1], James N. Palmer[1], Nithin D. Adappa[1], Noam A. Cohen[1], Michael A. Kohanski[1], Hong Wang[2], Jennifer E. Douglas[1]

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Background: Olfactory dysfunction (OD) is frequently observed in patients with chronic rhinosinusitis with nasal polyps (CRSwNP), a condition characterized by type 2 inflammation. Although therapies targeting type 2 cytokines (IL-4, IL-5, IL-13) have been shown to improve olfaction, the underlying mechanisms remain unclear. We examined the impact of type 2 cytokines on the olfactory epithelium (OE) using a novel human olfactory organoid model. Methods: Olfactory organoids were generated from the human superior turbinate tissue of non-CRS patients. Organoids were treated with 50ng/ml IL-13 for 24 hours, 48 hours, and 7 days. Odorant (geraniol and eugenol)-evoked calcium responses were measured to assess the activity of olfactory sensory neurons (OSNs). Peak responses (F/F0) were measured and compared across groups using unpaired t-test to evaluate the effect of cytokine exposure on OSNs. Results: Exposure to IL-13 induced a significant reduction in odorant-evoked peak responses at 24 hours ($p<0.0001$), 48 hours ($p=0.0017$), and 7 days ($p=0.003$) timepoints compared with control cultures, indicating an impairment of OSNs. Control cultures exhibited the expected baseline response to odorants at all time points. Conclusion: Human olfactory organoids can be used to investigate downstream implications of type 2 inflammatory mediators on human OE and OD in a species-specific manner. These cytokines appear to disrupt the function of OSNs. Further investigation is warranted to better understand the role of type 2 cytokines in OD and associated changes in OE architecture and gene expression.

225 **Compounded Effects Of E-Cigarette Aerosol Components On Glomerulus Size And Sniffing Patterns In Mice"**

Sean O'Sullivan, Farhan Augustine, Virginia Murray, Kafui Ameko, Iskandar Nassar, Silvi Shah, Setutsi Abdallah, Tatsuya Ogura, Weihong Lin
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Electronic cigarette (e-cigarette) usage is a growing activity among teens and young adults, with millions engaging in daily use. Aerosols produced by the combustion of e-cigarette liquids release flavorants along with harmful chemicals such as formaldehyde, toluene, other volatile hydrocarbons, and metals which can interact with the olfactory system through first and secondhand exposure. We previously observed aerosol exposure from e-cigarette liquids (e-liquids) with spiked heavy metals, simulating long-term vaping, reduced olfactory epithelium thickness, numbers of mature olfactory neurons, and glomerulus sizes. Following this, we investigated what the flavor components of e-liquid affect the specific glomerulus which senses a particular odor and how sniffing behavior of said odors was altered. Groups of mice were exposed twice daily for 8 weeks to simulate subchronic e-cigarette use, during which we assessed sniffing behaviors of e-liquid components at 0/4/8 weeks, following with harvesting and imaging olfactory bulbs from the mice. Exposure conditions consisted of air, propylene glycol/vegetable glycerin (PG/VG), PG/VG based e-liquid containing nicotine and OR151/M71 agonists, and e-liquid spiked with heavy metals. We observed that repeated exposure to e-liquid with the agonists induced increased size of the cognate glomerulus, but spiking the e-liquid with metals decreased size. Furthermore, both e-liquid exposure groups showed markedly less interaction times with e-liquid components. These findings suggest that repeated e-cigarette exposure reduces sniffing behavior and corresponding ligand glomerulus size, possibly due to toxic effects of the aerosol and/or desensitization to the odorants in the aerosol.

227 **Il-13 Drives Signaling Pathways And Chitinase Expression In Human And Mouse Olfactory Stem Cells**

Yuchen K. Sun, Binbin Ma, Haiqing Zhao, Andrew P. Lane
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Background: Olfactory loss is common in chronic rhinosinusitis with nasal polyps (CRSwNP) and tracks with type-2 (T2) inflammation. In the olfactory epithelium (OE), horizontal basal cells (HBCs) are quiescent stem cells that activate after injury. We examined HBC responses to interleukin-13 (IL-13) in human-relevant models. Methods: We used a mouse line with inducible, OE-specific IL-13 and performed single-cell RNA-sequencing,

pathway enrichment, and immunostaining. Ex vivo, human HBCs isolated from olfactory brushings (controls, CRS, CRSwNP) were stimulated with IL-13 and analyzed by gene expression and immunostaining. Results: In mice, IL-13 drove HBC-centric transcriptional programs linked to activation and immune crosstalk, including apoptosis, JAK–STAT3, and PI3K–AKT signaling. IL-13 robustly upregulated the chitinase-like protein Ym2 (Chi3l4) in HBCs, globose basal cells, and sustentacular cells. In human HBCs, IL-13 increased acidic mammalian chitinase (CHIA) mRNA, with greater induction in CRS/CRSwNP donors than controls, accompanied by NOTCH1 and STAT3 upregulation. The CHIA response echoes murine Ym2, indicating a conserved chitinase-linked pathway in HBCs under T2 conditions. Conclusions: Across mouse and human systems, IL-13 activates signaling and chitinase programs in olfactory HBCs—Ym2 in mice and CHIA in humans—suggesting T2-specific engagement of epithelial immune defenses by OE stem cells, potentially at the expense of sensory maintenance. These pathways nominate candidate biomarkers for CRSwNP-related olfaction loss.

229 **Upregulation Of Alzheimer&Rsquo;S Disease-Related Genes In The Olfactory System Following Influenza Virus Infection**

Elias Mimouni[1,2], Akihito Kuboki[1], Shaina Maitra[1,3], Cailu Lin[1], Danielle R. Reed[1], Peihua Jiang[1], Johannes Reisert[1], Haiqing Zhao[4], Hong Wang[1]

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Loss of smell is one of the earliest symptoms observed in Alzheimer's disease (AD), often preceding cognitive decline by several years, suggesting that the olfactory system may play a role in early disease pathogenesis. Viral infections, including influenza, have emerged as potential risk factors for AD and may modulate neurodegenerative pathways. However, the mechanisms linking peripheral viral infection to AD remain poorly understood. We previously demonstrated that influenza viruses can directly infect olfactory sensory neurons and induce smell loss in a mouse model. In the present study, we examine whether influenza virus infection alters the expression of AD-related genes in the olfactory epithelium (OE) and olfactory bulb (OB). RNA was isolated from the OE and OB of uninfected control mice and mice at 7, 14, and 30 days post-inoculation (dpi). RNA sequencing and quantitative RT-PCR were performed to assess gene expression changes. We observed upregulation of multiple inflammatory pathways in both the OE and OB, notably the upregulation of complement components involved in synaptic pruning. Influenza virus infection also increased the expression of *Mapt* and *App*, which encode Tau and amyloid precursor protein, respectively, two proteins whose dysregulation contributes to AD pathogenesis. Furthermore, several genes encoding kinases that phosphorylate Tau, including *Mark1*, *Ttbk1*, and *Ttbk2*, were significantly upregulated in olfactory tissues. Tau hyperphosphorylation is a critical step leading to Tau misfolding and the formation of insoluble filaments within neurons, a key pathological hallmark of AD. Together, these findings indicate that influenza virus infection induces AD-related pathways, particularly those associated with Tau phosphorylation, in the peripheral olfactory system.

231 **Incidence Of Smell Loss In Patients With Allergic Fungal Rhinosinusitis: A Single-Center Retrospective Chart Review**

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Background: Allergic fungal rhinosinusitis (AFRS) is a distinct subtype of chronic rhinosinusitis with nasal polyps (CRSwNP), the leading cause of olfactory loss. Despite both having the presence of polyps, AFRS tend to present as a unilateral disease and occurs most frequently in younger males and African Americans. AFRS occurs almost exclusively in the southeastern US, due to the warmer, more humid climate which is optimal to fungal growth. Although smell loss is one of the cardinal symptoms of CRSwNP, it has not been described in AFRS patients, and thus the focus of these studies. Methods: Single-center, retrospective chart review of a total of 815 patients enrolled from February 2021 to December 2025 was conducted. Olfactory function was evaluated using the UPSIT. Subjective disease severity was measured by the validated SinoNasal Outcomes Test-22 questionnaire (SNOT22), Patients under 18 years of age or possible malingering results in their UPSIT were excluded. Results: AFRS patients have a statistically significant lower UPSIT scores when compared to control and CRSsNP. The degree of olfactory loss was equal to CRSwNP. More than 90% of AFRS patients experience some degree of olfactory loss, with 32.5% experiencing total anosmia. AFRS patients also had a significant worse SNOT22 score compared to control and CRS without polyps (CRSsNP) patients, showing worse subjective disease severity. Conclusion: Patients with AFRS has a similar degree of olfactory loss compared to patients with CRSwNP, and significantly worse than control and CRSsNP patients. This is particularly interesting given AFRS typically presents as unilateral disease while CRSwNP is bilateral. This suggests that inflammation, and not air flow obstruction, may be responsible for CRSwNP and AFRS-related olfactory loss.

233 **Study Of Chemosensory Enhancement Through Neuromodulation Training (Scent) For Long Covid: A Blinded Interim Analysis**

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

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Few evidence-based treatments exist for COVID-related persistent smell dysfunction. While smell training (ST)

shows preliminary efficacy and is an often-prescribed intervention, additional study is required. Our research team is conducting a large, at-home, randomized, controlled trial of ST and trigeminal nerve stimulation (TNS)-enhanced ST for the treatment of Long COVID-related disturbances in smell, mood, sleep, and cognitive function. A planned treatment-blinded, interim analysis was conducted to assess initial acceptability and feasibility of the interventions. Thus far, sixty-four (50 female) adult participants ($Age_{M\pm SD} = 47\pm10.93$) have been randomized into one of three treatment arms, ST, TNS-enhanced ST, or placebo ST. Forty-five participants have completed all 12-weeks of treatment and all follow-up assessments (i.e. study completers), with eleven participants still in treatment and a relatively low attrition rate, i.e. eight participants (12.5%). As a group, the study completers trained an average of 50.53 of the 60 assigned training days (~84.22%); only 4 of the 45 study completers did not meet the treatment goal of completing at least 80% of all training sessions. The study interventions were assessed using the Acceptability and Feasibility of Intervention Measures (AIM and FIM, respectively), which queried whether the treatment "is easy to use" and "will work", for example. Scores for the AIM (M±SD=4.29±0.86) and FIM (M±SD=4.55±0.60) in the group of study completers exceeded the threshold of 4, indicating adequate feasibility and acceptability. Overall, ST and TNS-enhanced ST appear to be suitable treatments that are easily implemented into daily life. Future interim analyses will explore these measures alongside initial efficacy across the blinded treatment arms.

235 **Activation Of Horizontal Basal Cells In The Oe Restores Neurogenesis After Neurogenic Exhaustion Sets In**

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Age-related anosmia and postinfectious olfactory dysfunction afflict millions of individuals, but effective molecular therapies are lacking. Progress toward their development requires animal models that mimic the pathology of the human olfactory epithelium (OE). Here, we introduce a highly efficient, genetically encoded neuron-specific ablation platform based on OMP–driven expression of Nitroreductase 2.0 (OMP-NTR) in mature olfactory sensory neurons (mOSNs). The administration of metronidazole, which the enzyme converts to an intracellular toxin, causes the rapid, reversible, and temporally precise elimination of mOSNs. In the short-term, despite the complete ablation of mOSNs, the epithelium's neuroregenerative capacity remains intact. However, chronic accelerated neuronal turnover drives progressive regenerative failure that closely phenocopies human olfactory aging at the histological level, including neural stem cell exhaustion, aneuronal OE, respiratory epithelial metaplasia, and persistent anosmia. Horizontal basal cells (HBCs) remain extant in the degenerated OE and are a therapeutically attractive stem cell reservoir. Although HBCs are dormant in the unlesioned OE or in the setting of abbreviated neuronal lifespan (as seen after olfactory bulbectomy or with the OMP-NTR model described here), HBCs can be activated after olfactotoxin injury to make globose basal cells (the active neuronal stem cells and progenitors) and non-neuronal cells. Our findings demonstrate that targeted downregulation of the master transcription factor, deltaNp63, in the OMP-NTR pathological setting activates HBCs, restores neurogenesis, and promotes reinnervation of the olfactory bulb. This work provides the proof-of-concept for a molecularly defined therapeutic strategy to reverse olfactory dysfunction.

237 **Prognosis Of Chemosensory Recovery Among Long Covid-19 Patients - Objective Assessment At 3, 6 And 12 Month Follow-Ups**

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This ongoing study evaluates chemosensory recovery following post-acute sequelae of SARS-CoV-2 infection (PASC). 37 subjects aged 30-84 (median: 57) who had contracted COVID-19 from February 2020 and October 2024 or 8 to 62 months (median: 37) were recruited. Patients received objective testing of 1) olfactory function using the 9-Item NIH Toolbox Odor Identification (ID) Test, odor detection threshold (ODT) to phenyl-ethyl alcohol (PEA); 2) taste function using the modified NIH toolbox; 3) chemesthetic function using menthol lateralization thresholds. All then completed a 3-month follow-up, while 22 completed a 6-month follow-up, and 16 completed a 12-month follow-up. At the initial visit, patients self-reported a high prevalence of smell (86%) and taste (73%) losses, with 62.5% of patients with confirmed objective smell loss, 81% with objective trigeminal losses, while only 15% confirmed objective taste loss. At the 3 and 6-month follow-up, patients exhibited significant improvements in objective smell (Odor ID, $p<0.05$), especially among patients with initial smell complaints, yet objective chemosensory losses remained high: at 3-month follow-up: smell 41%, taste 22%, nasal trigeminal 81%; 6-month follow-up: smell 59%, taste 27%, nasal trigeminal 82%. At the 12-month follow-up, 44% continue to exhibit smell loss, 63% trigeminal losses, while only 38% taste losses.These findings suggest significant fluctuation in chemosensory function following COVID-19 infection, with prognosis prolonged and uncertain, and self-report being unreliable, especially for taste loss.

239 **Mobility, Physical Activity, And Social Activity Impairments, Particularly In Male Apoe E4 Carriers, Are Associated With Olfactory And Cognitive Dysfunction**

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Important studies have revealed that olfactory dysfunction is associated with poorer quality of life (QoL). Those studies were primarily associated with ingestion. Here we focused on issues related to cognitive decline. The devastating impact of Alzheimer's Disease (AD) necessitates developing intervention strategies targeting modifiable risk factors. QoL impairments may be associated with cognitive and olfactory dysfunction in preclinical AD and represent potential modifiable risk factors. We analyzed data from the 548 adults 60+ yrs from the Rancho Bernardo Study who had both National Geographic Smell Survey assessments and genetic testing for ApoE ε4 status, a genetic predictor of AD risk. They were assessed with the Mini Mental Status Examination and Quality of Well-Being Scale. QoL domains included overall functioning and specific impairments in physical activity, social activity, and mobility. In this baseline analysis multivariate linear regressions examined associations between QoL impairments, cognitive and olfactory function, controlling for age, sex, education, and antidepressant/anxiolytic use. Lower overall functioning, physical and social activity impairments were associated with olfactory dysfunction. In females, social activity and mobility impairments related to olfactory dysfunction. Male ε4 carriers with greater social and mobility impairments had worse olfactory function. Findings that mobility, physical activity and social activity impairments, especially in male ε4 carriers, are associated with olfactory and cognitive dysfunction suggest the need to investigate the direction of the effects and the potential for interventions. Further research is warranted to investigate underlying mechanisms and predictive value for future decline. NIH support: R01AG004085; R01AG062006 (CM)

241 **Novel 3D Printed &Ldquo;Smell-Aids&Rdquo; To Improve Olfactory Function In Post Covid-19 Era**

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We previously invented non-invasive "Smell-Aids" to improve olfactory function by enhancing intranasal odorant delivery to the olfactory epithelium. However, the initial design was hand-made foam nasal plugs, lacking professional appearance, consistency, and scalability. Here, we attempted to update the prototype fabrication using 3D printing. 2 plug sizes were designed to accommodate different nostril sizes, each incorporating diagonal airflow channels of either small (5mm) or large (7mm) diameters. These updated designs were then 3D printed using the Formlabs Form 3 SLA printer with Silicon 40A photopolymer resin. We tested the prototypes in counter-balanced orders on 18 patients with confirmed olfactory losses (age 19-89y, median=62), majority of whom (11/18=61%) were non-COVID smell losses spanning 3m-19 years. The remaining were post-COVID long haulers (n=7; infected 11/26/20 to 3/11/24; persisted 10 to 61 months, median=52m). All patients achieved comfortable fit with at least one plug size. The 9-item NIH toolbox odor identification score significantly improved with the large channel (7mm) in the upward direction (baseline: 3.2±1.99 vs plug: 4.0±2.03, $p<0.05$), especially among the non-COVID cohort (2.6±1.99 to 3.6±2.03, $p<0.05$). No significant improvement was observed with the plug downward direction nor with small diameter plugs. Subgroup analysis on patients who reported distorted smell (parosmia/phantosmia 4/18) showed no significant effect. These results further demonstrated the promise of improving olfactory function through peripheral mechanisms with efficacy depending on the amount of air/odor flow (large channel) redirected to the olfactory region and different patient cohorts.

243 ***The Knowswatch: Concept And Prototype For A Wearable Chemosensory Sensing Device***

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Purpose: In two studies examined were the needs of patients regarding the electronic olfactory sensor, and one potential use of prototypic device. Participants with olfactory disorders provided information on situations that are most impaired due to olfactory disfunction, and their expectations of the sensor. Prototypic smartwatch that knows by smell (KnowsWatch) was trained to distinguish spoiled meat and fish from the fresh, and achieved good accuracy in laboratory environment. Methods: Participants with olfactory disorders completed a questionnaire regarding impaired situations and sensor expectations. Their needs were then answered with proper training of the KnowsWatch – electronic nose in a form of a smartwatch. Results: Around half of the participants expressed interest in using KnowsWatch in their daily lives. Most prevalent mentions of desired functions were detection of smoke and gas, recognition of spoiled food, and personal hygiene. KnowsWatch was trained to recognize spoiled and fresh meat and fish and achieved very good accuracy in the laboratory environment. Conclusion: As participants with olfactory disorders express the need of assistance in some olfactory-related daily situations, the KnowsWatch could be good answer to their queries. Prototypic device answers some of mentioned expectations and proved to be efficient in laboratory testing. It is now time to test in in real-life situations.

245 **Adhering To Healthy Plant-Rich Diets Is Associated With Better Olfactory Function In The General Population - Findings From The Cooperative Health Research In South Tyrol (Chris) Study**

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Olfactory dysfunction is associated with increased all-cause mortality among older adults and an early

indicator of brain aging. Different lifestyle factors and health conditions determine olfactory function, however, there is limited knowledge on the association with diet quality. We investigated the association between various dietary patterns and olfactory function, as well as hyposmia, in a general population study using cross-sectional data from more than 6000 participants of the Cooperative Health Research in South Tyrol (CHRIS) study. We assessed self-reported dietary intake through the GA^{2}LEN semi-quantitative Food Frequency questionnaire, which was used to derive five established dietary pattern indices (Alternate Healthy Eating Index 2010, Mediterranean diet index, Plant-based dietary index, Healthy Plant-based dietary index, Unhealthy plant-based dietary index), as well as various food groups. Olfactory function was measured through the Sniffin'Sticks odor identification test, which allowed us to determine hyposmia with a score >12/16. Multivariable ordinal and logistic regression models were fitted to investigate associations between each dietary pattern, food groups and olfaction. Higher adherence to all healthy dietary patterns was associated with both better olfactory function and lower rates of hyposmia, while the opposite was observed for the unhealthy plant-based diet. Specifically, higher consumption of fruits, vegetables, coffee and tea was beneficially associated with both outcomes. Higher adherence to healthy dietary patterns that are rich in plant-based foods was associated with better olfactory function and lower rates of hyposmia.

247 **Validation Of Scentinel 2.0 Against Three Established Olfactory Measures**

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While validated tests like 9-item NIH Toolbox Odor Identification test (NIHTOI), and the 12-item Brief Smell Identification Test (B-SIT), and 16-item Sniffin' Sticks Odor Identification test (SS-I) accurately measure olfactory function, their length, cost, and requirement for trained administrators limit population-wide screening. SCENTinel is a rapid, self-administered screening tool that measures odor detection, identification, intensity, and pleasantness using one odor at the time, offering a scalable alternative. We validated SCENTinel's performance in detecting smell dysfunction in a sample of 363 individuals aged 18-83 (mean: 44±19 years old) who completed all tests in one session along with demographic and health surveys. Across 9 odor versions, SCENTinel demonstrated excellent specificity (mean ≈ 0.97-0.99) and precision (mean ≈ 0.73-0.83), but lower sensitivity (mean ≈ 0.21-0.28) in detecting smell dysfunction. Fair-to-moderate agreement with gold standards ($\varkappa$ ≈ 0.25–0.34) was comparable to agreement among the reference tests themselves ($\varkappa$ ≈ 0.28–0.42). Test-retest reliability for SCENTinel was similar to NIHTOI, supporting temporal stability. SCENTinel provides 3 times faster and 2.5 times less expensive, reliable, conservative detection of smell dysfunction, supporting its use as a rapid, low-burden screening tool for population-level olfactory surveillance.

249 **The Sense Of Smell Is Not Idiosyncratic**

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Human olfaction is considered idiosyncratic. Here we tested the alternative hypothesis that people are not uniquely different in their sense of smell, but instead show individual variability comparable to that observed in vision. Sixty participants rated similarity between pairs of odorants and pairs of images. Stimuli spanned high, medium, and low similarity: odorants based on angular distance in physicochemical space, and images from the THINGS dataset. In a subset (n=30), the same stimuli were used in a 1-back fMRI paradigm. We quantified within-subject and between-subject variability in similarity judgments. Within-subject variability (mean within-pair range) was nearly identical for odors and images in both the full cohort and fMRI subset (all $p \geq 0.32$, $|d| \leq 0.16$, $BF_{01} \approx 3.7–4.8$). Two one-sided equivalence tests (TOST) with a ±5-unit margin confirmed equivalence in both cohorts (all $p < 0.001$). For between-subject variability, a globally matched odor–image set was analyzed. Across-participant standard deviation did not differ significantly between modalities (paired tests $p \geq 0.18$, $d \leq 0.57$, $BF_{01} \approx 0.87-2.1$), and TOST supported equivalence within ±5 SD units in both cohorts (all $p \leq 0.033$). The fMRI data dovetailed with the behavioral data: inter-subject variance of neural representational dissimilarity matrices (RDMs) within modality-specific cortical regions was similar across systems (mean variance: olfaction=0.04, vision=0.065, P=NS), and a universal similarity representation regardless of modality was uncovered in the angular gyrus. Taken together, these results imply that the concept of perceptual similarity stably spans sensory systems, and humans are not more different from each other in their olfactory representations than in their visual representations.

251 **Characterization Of Olfactory Event-Related Potentials In Subjective Cognitive Decline**

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Olfactory loss is a recognized feature of Alzheimer's disease (AD) and is believed to be among its earliest indicators. However, the characterization of olfactory function in Subjective Cognitive Decline (SCD), an early

preclinical stage on the AD continuum, remains limited, with olfactory changes often subtle and difficult to detect using behavioral measures alone. Olfactory event-related potentials (OERPs) provide a well-controlled neurophysiological approach to assessing distinct components of olfactory processing that may be sensitive to changes not yet reflected in behavioral performance. The aim of this study was to characterize OERPs in individuals with SCD. A total of 95 participants aged 60 years and older were recruited, including 50 individuals with SCD (34 women) and 45 healthy controls (30 women). Brain activity was recorded using a 32-electrode EEG system while participants received two independent blocks of 40 chemosensory stimulations delivered by an olfactometer (Burghart OL023). Phenyl ethyl alcohol (PEA) was used as the pure olfactory stimulus of interest, whereas carbon dioxide (CO_2) served as non-olfactory (trigeminal) control stimulus. Early (N1) and late (P2/P3) OERP components were measured in terms of latency and amplitude. Mixed-design ANOVAs were conducted to compare groups across component measures and stimulus conditions. The SCD group showed longer latencies for late components (P2/P3) specifically in response to the odorous stimulation. No group differences were observed for N1 latency, nor were any differences found in the amplitudes of early or late components. These findings suggest that olfactory processing alterations may already be evident very early in the AD continuum. Such alterations are reflected in our study by delayed latencies at later processing stages

253 **Coupling Of Neural Oscillations In Cortical Networks During Odor Intensity Perceptual Decisions**

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Intensity is a fundamental aspect of perception. How brains code for intensity of olfactory stimuli is an open question. We have been studying how neural oscillations in piriform cortex might code for perceived odor intensity. We presented odors, using consistent concentration sampling bags, to patients undergoing intracranial EEG monitoring for epilepsy, using 3 concentrations of 3 odors, in addition to clean air. Participants gave an intensity rating on each trial, while we obtained high resolution LFP recordings from electrode contacts implanted throughout the brain. Preliminary data suggest gamma oscillations (30–60 Hz) in piriform cortex are stronger and last for longer duration during sniffs of strong odors, shown by comparisons of significant increases of gamma oscillations measured during strong vs. weak intensity rated trials (permutation test against pre-sniff baseline, FDR-corrected). Furthermore, machine learning approaches suggest the gamma signal is representing perceived intensity rather than concentration. This task relies not only on perception of the intensity of odors but also holding that percept in mind in order to make an accurate rating each trial, implicating areas beyond piriform cortex. The olfactory bulb is bidirectionally connected to piriform cortex and several other limbic and cortical areas, including amygdala, orbitofrontal cortex, cingulate cortex, and insula. While we continue to investigate oscillatory coding for perceived odor intensity in piriform cortex, this poster will highlight explorations of how coherent neural oscillations emerge across olfactory cortical and limbic areas, as potential mechanisms for coordinating discrete neural networks for odor perception.

255 **Olfactory Meta-Cognition Is Altered In Individuals With Anxiety And Depressive Symptoms**

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People experiencing anxiety and depressive symptoms perceive odors differently than healthy individuals. Depending on the mental disorder, olfactory sensitivity might be decreased or elevated. However, compared to psychophysical investigations, insights into meta-cognitive aspects of olfactory processing are poorly investigated in people with mental disorders. In a series of two studies, we verified how symptoms of generalized anxiety, social anxiety, depression, and olfactory reference disorder (ORD) are related to olfactory meta-cognition (body odor sniffing frequency, odor awareness, body odor disgust). Study 1 (n=215, M_{age}=21.82, SD_{age}=6.45, 136 women, Australian) demonstrated that social (r=.16) and generalized (r=.17) anxiety symptoms, but not depressive symptoms, are weakly but significantly related to frequency of body odor sniffing. Study 2 (n=288, M_{age}=27.3, SD_{age}=9.9, 186 women, Polish) partially replicated these findings showing relationship between social anxiety and body odor disgust (r=.20); generalized anxiety, odor awareness (r=.24), and body odor sniffing (r=.20); as well as between ORD, odor awareness (r=.24), body odor sniffing (r=.20), and body odor disgust (r=.23). Taken together, these findings demonstrate that mental disorder symptoms are associated not only with altered olfactory sensitivity but also changed meta-cognitive aspects of smell perception. The role of altered olfactory meta-cognition in emergence and maintenance of mental disorders awaits further investigation.

257 **Cirano: A Large Language Model For Generating Odor Descriptions From Molecular Structure**

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Recent advances in deep learning have enabled prediction of odorant perception from molecular structure, opening new avenues for odor classification. However, most existing models are limited to predicting percepts from fixed vocabularies and fail to capture the full richness of olfactory experience. Progress is further limited by the scarcity of large-scale olfactory datasets and the lack of standardized metrics for evaluating free-form natural-language odor descriptions. To address these challenges, we introduce Odor Description and Inference Evaluation Understudy (ODIEU), a benchmark which includes perceptual descriptions of over 10,000 molecules paired with a model-based metric for evaluating free-form odor text descriptions. The model-based metric uses Sentence-BERT (SBERT) models which are finetuned on olfactory descriptions to allow better evaluation of human-generated odor descriptions. Using the finetuned SBERT models, we show that free-form text odor descriptions contain additional perceptual information in their syntactic structure compared to semantic labels. We further introduce CIRANO (Chemical Information Recognition and Annotation Network for Odors), a transformer-based model that generates free-form odor descriptions directly from molecular structure, thus implementing the molecular structure-to-text (S2T) prediction. CIRANO achieves performance comparable to humans. Finally, we generate human-like descriptions from mouse olfactory bulb neural data using an invertible SBERT model, yielding neural-to-text (N2T) predictions highly aligned with human descriptions. Together, CIRANO and ODIEU establish a standardized framework for generating natural language olfactory descriptions and evaluating their alignment with human perception.

259 **Olfaction Benchmark For Large Language Models**

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We introduce the olfactoion benchmark, a standardized, multi-task evaluation of large language models on diverse set of problems in olfaction and odor reasoning. The benchmark spans diverse capabilities, including odor classification and descriptors, perceptual attributes including intensity and pleasantness, olfactory perception, receptor activation, and multi-label semantic profiling, with different prompting procedures. We evaluate a broad set of state-of-the-art commercial and open-source models and assess performance in both aggregated performance and fine-grained analyses of error patterns. To probe robustness beyond English, we extend subset of benchmark to a multilingual setting via translated prompts and compute performance across languages and models. Our results provide a high-level map of current LLM strengths and limitations in olfactory intelligence and establish a reproducible framework for tracking progress in sensory reasoning.

261 **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? In this poster we will present an ambitious multi-center project (Israel-Sweden-Germany) funded by an ERC Synergy grant where we address these basic questions. We have 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 be by a series of rating scales, and an option to photograph the odor source. By probing 24,000 participants 4 times a day we will obtain nearly 1 million ratings, reflecting coverage of ~1000 ratings per minute of wake. So far, after recruiting more than 3,500 participants (out of the 24,000 planned), our data suggests that people perceive smell about 15% of their wake time. Food is by far the most perceived smell, flowed by coffee and perfume. Additionally, it seems that around 12:30 and 20:00 people are most aware of smells, a pattern that may be heavily affected by meal times. Both age and sex showed significant effects on reporting, where men reported more smelling events than women ($\chi^2(1) = 25.32$, $p < .0001$) and people in their 30's showed the highest smell awareness reports ($\chi^2(3) = 81.80$, $p < .0001$).We are in the midst of gathering data from many countries, such as Isreal, Germany, Sweden, UK, Uganda and many more to come.

263 **Standardizing A Universal Scale For Odor Intensity**

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In vision and hearing, standardized units such as lumens and decibels allow consistent quantification of stimulus intensity, enabling precise control of sensory experiences. Olfaction, by contrast, lacks a robust quantitative framework for odor intensity, complicating efforts to accurately characterize and compare aromas across laboratories. To bridge this gap, we used a precisely controlled odor delivery system to estimate the concentration-intensity function and Weber fraction (normalized just-noticeable-difference) of the ASTM standard odorant, n-butanol. Using this information, we built a universal scale for odor intensity. We demonstrate its utility by mapping synthesized and natural odors on to this common metric. Using a larger dataset (N = 62 odorants), we further show that panels can easily calibrate to the scale using a simple linear transformation. This universal odor scale provides standardizes units to compare odor intensity across laboratories and offers a regulatory foundation for odor-related policies, including smell pollution control.

265 **Taking A Hint: Stimulus Investigation Shapes Taste Representation In Gustatory Cortex**

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Taste processing in Gustatory Cortex (GC) is dynamic, with neural taste responses passing through a series of characteristic coding states, but to observe these states effectively requires the high temporal resolution of electrophysiology. This functional requirement has previously necessitated either that rodents be head-fixed or that taste stimuli be delivered via intraoral cannula directly into the mouth, or both. However, the voluntary oromotor action of licking creates an immediate discontinuity in the physical dynamics of a stimulus encountered during free licking and stimuli delivered by IOC. As such, it is unclear whether the “dynamic model” of taste processing generalizes to responses evoked by the active licking of a freely-moving animal. An additional factor may prove even more consequential: stimulus investigation. Incidental olfactory cues available to freely-moving animals are likely to substantially alter dynamic responses in GC, allowing animals to identify stimuli and plan action before tasting the stimulus. In order to addesss both of these questions, we used a novel behavioral apparatus with controlled ventilation to facilitate electrophysiological recording during freely-moving licking while modifying the availability of olfactory cues. We were able to observe the anticipated dynamic responses in GC, though we found that allowing olfactory investigation of the stimuli altered the timing of those dynamics, aligning them with that cue investigation rather than taste onset. Additionally, we found that this shift was reversed by the removal of the olfactory cue.

267 **Cortical Chemosensory Responses To Taste And Smell**

Thomas Gray, Ainsley Craddock, Donald Katz
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In the experience of eating foods or drinking beverages, among other sensations, taste and smell often occur coincidentally. It’s understudied how the higher order cortical regions that process taste and smell interact. It is known that chemosensory cortical areas can respond to multimodal chemosensory stimuli such the gustatory cortex exhibiting both taste and odor stimuli responses but it is unclear whether the interactions and exchange of signals between these two areas influence these responses. Intertwined with this question is whether there is a coherent response occurring simultaneously in both of these regions and to what degree it depends on if smell is delivered retronasally (through the mouth) or orthonasally (into the nares). We demonstrate interactions of this chemosensory cortical network with dual site electrophysiological recordings, advanced imaging, and behavioral analysis.

269 **Cortical Dynamics In Primary Chemosensory Areas To Multimodal Stimuli**

Ainsley Craddock, Thomas Gray, Abuzar Mahmood, Donald Katz
Brandeis University

During feeding behaviors, taste and smell often coincide, creating the experience of flavor. While multiple components of this experience remain largely understudied, there have been considerable efforts to gain a better understanding for how chemosensory cortical areas work to process multimodal chemosensory stimuli. The higher order cortical areas responsible for processing taste, smell, and flavor are gustatory cortex (GC) and piriform cortex (PC). The computations that occur in these areas are beginning to become more characterized; however, dynamics between these areas have been relatively unexplored with regards to single-unit resolution electrophysiology. As demonstrated in our electrophysiological data, not only do GC and PC interact dynamically when a combination of taste and smell are given to rats, but each area also contains populations of neurons responsive to both stimuli. A question that remains is how the coherence between GC and PC is modulated when unimodal or multimodal stimuli are perceived, and whether this coherence depends on the method of odor delivery (retronasally through the mouth, or orthonasally into the nares). To answer this, we delivered stimuli in a pseudorandom order, both passively and actively, while simultaneously recording in GC and PC. Additionally, we demonstrate the effects of modulating these afferent connections from PC to GC using optogenetics in order to determine the dependence of GC odor responsive neurons on PC neuron populations. This work aims to address gaps in chemosensory cortical dynamics by recording these two areas simultaneously in freely moving rats and perturbing normal responses in chemosensory neurons.

271 **Auditory And Visual Object Processing In Olfactory Cortex Of Individuals With Life-Long Olfactory Deprivation**

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The traditional view of modality-specific brain organization has been challenged by demonstrations of cross-modal processing, i.e. the activation of specialized sensory cortex by input from other senses. An alternative theory suggests that rather than specializing in different sensory modalities, different parts of the cortex can specialize in different types of tasks. We recently addressed this question in the olfactory domain, showing that in normosmic individuals, the primary olfactory cortex (piriform cortex) responds to unimodal auditory and visual objects, regardless of how strongly they are associated with an odor. Here, we assess whether previous olfactory experience is a prerequisite for this cross-modal processing, using a unique group of individuals born without a sense of smell (congenital anosmia; CA; $n = 30$). First, we confirmed the presence of clear visual and auditory activations in the piriform cortex of the sensory deprived individuals. As compared to normosmic controls ($n = 30$), these activations and associated functional connectivity, both within the piriform cortices and between piriform cortex and other regions, were altered in a modality dependent way. Our results show that life-long absence of olfactory input does not impede cross-modal activations by visual and auditory objects in the piriform cortex and are compatible with the idea of a task-based rather than modality-specific organization of this brain region.

273 **Investigating Attention-Gated Rule Representations Using An Olfactory Selective Attention Task**

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To make adaptive decisions in complex, multisensory environments,the brain must form and maintain task representations that are specific to selectively attended sensory cues. Animal research has demonstrated that multivariate task rule representations in prefrontal cortex (PFC) are linked to sensory cues via attention-gated input from the thalamus. However, the relationship between the rule representations in PFC and attention-modulated thalamic connectivity in humans is not well described. Here we investigate this question using a bimodal two-alternative forced choice task and ultra-high field fMRI in humans. On each trial of this task, participants are cued to attend to either olfactory or auditory stimuli, before simultaneous delivery of one of two distinct odors and one of two distinct tones. The identity of the attended stimulus determines the unique response rule involving two correct and two incorrect choice options. Behavioral results revealed significantly worse performance on olfactory attention trials and above-chance performance across conditions. We predict that connectivity between the thalamus, primary olfactory cortex, and primary auditory cortex will be promoted or suppressed based on selective attention to salient stimuli from the corresponding sensory modality. We further hypothesize that attention-modulated connectivity states will precede the emergence of rule-specific patterns of PFC activity. This would provide evidence that the thalamus initiates an attention-gated cascade of neural activity to promote rule representation in downstream prefrontal cortices, and thus shed light on how the neural representation of behavioral rules is linked to external stimuli via selective attention.

275 **Temporal-To-Spatial Code Transformation In The Piriform Cortex**

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Odor identity is represented by temporal sequences of glomerular activation in the olfactory bulb (OB). One potential function of cortical networks is to decode these sequences to infer odor identity. Chunking models have been proposed to transform a temporal latency code into a spatial representation in the piriform cortex. One prediction of these models is that each piriform neuron has a specific time window within the sniff cycle during which it is responsive to OB inputs, aka the Bulbar Sensitivity Window (BSW). BSW onset is determined by the amount of inhibition received by the piriform neuron: the stronger the inhibition, the later the neuron responds. BSW onset does not depend on odor identity. Due to recurrent circuitry in the cortex, blocking the activation of earlier cortical neurons prevents the activation of later ones. In the simplest form of the chunking model proposed before, the BSW never closes - neurons remain responsive to OB inputs from their onset time until the end of the sniff cycle. Recent data from the piriform cortex suggests that BSW closes before the end of sniff cycle. Here, we propose two mechanisms by which the BSW can be closed. First, inhibition from later-activated cortical neurons may desensitize earlier cells, thereby closing their BSW. This mechanism implies that, in addition to the feedforward excitatory circuitry proposed in earlier models, cortical circuits exhibits biased feedback inhibition. Second, feedback from the cortex to the OB may selectively inhibit inputs to earlier piriform neurons, implementing a form of predictive coding. Together, these two theoretical models implement temporal-to-spatial code transformation in the piriform cortex while accounting for recent cortical data. Both models make specific, testable predictions about cortical circuitry.

277 **Mimicking Dose-Response Experiments To Predict Olfactory Receptor Activity And Potency**

Matej Hladiš[1,2], Maxence Lalis[2], Michael Bronstein[1,3], Jérémie Topin[2]

[1]University of Oxford, Oxford, United Kingdom, [2]Université Côte d'Azur, Nice, France, [3]AITHYRA, Vienna, Austria

The mammalian sense of smell can distinguish a myriad of odors using a complex code consisting of interactions

between odorant molecules and hundreds of different olfactory receptors (ORs). Beyond olfaction, these proteins are emerging as novel therapeutic and diagnostic targets for diseases such as obesity, diabetes, asthma, and cancer. Two key properties that characterize both the odor coding and the druggability of ORs are activity and potency (i.e. half maximal effective concentration, EC_{50}). In this work, we propose a novel paradigm for modelling these properties. Our approach, called ASMI-DR, achieves an EC_{50} estimation error of 0.725 log units under random data splits and below 1 log unit in challenging out-of-distribution evaluations, outperforming several state-of-the-art regression baselines by more than 40%. To achieve these results, we mimic *in vitro* dose-response assays. Specifically, we design a novel model that learns the activation probability $P(s, m| c)$ for a given protein-molecule pair (s, m) at a concentration c. Then by querying this model at concentrations spanning several orders of magnitude, we fit a logistic curve to derive activity (the curve's maximum) and EC_{50} (the curve's inflection point) in a unified framework. Evaluated on the challenging M2OR dataset with test sets of approximately 1100 OR-molecule pairs, our framework achieves state-of-the-art performance for activity prediction and significantly improves EC_{50} estimation, outperforming drug–target regression baselines and exceeding the affinity module of Boltz-2 by 0.385 log units. Notably, ASMI-DR successfully identifies novel active molecular scaffolds, highlighting its potential to substantially reduce reliance on costly *in vitro* primary screening.

279 **Quantification Of Fluorescence Responses In A Newly Developed, Dryable Cell Line Expressing Odorant Receptors**

Andisheh Balouchi[1], Redwan Haider[1], Roy Anderson[1], Richard Cornette[2], Takahiro Kikawada[2], Ricardo Araneda[1], Elisabeth Smela[1]

[1]University of Maryland, College Park, MD, United States, [2]NARO, Tsukuba, Japan

Olfactory sensors are powerful tools for potential applications in diverse fields from environmental monitoring to medical diagnostics. Specifically, cell-based sensors utilizing insect odorant receptors (ORs) show great potential capability to detect and distinguish odors. However, the limited durability of living cells outside aqueous culture conditions constrains the sensor's storability and function. To overcome this issue, we utilized a novel desiccatable cell line Pv11, derived from *Polypedilum vanderplanki*, which can survive complete dehydration and storage in the dry state for over a year. The Pv11 cells were engineered to express a specific *Drosophila melanogaster* OR (Or47a) with its corresponding co-receptor Orco and the intracellular calcium indicator GCaMP6f. In our previous study, we demonstrated that Pv11-Or47a cells respond to their cognate ligand, pentyl acetate (PA), 12 hours after rehydration, in a dose-dependent manner and to repeated exposures. Here, we improve quantification of fluorescence responses in Pv11 cells by normalizing readouts to viable cells using Hoechst 33342 to stain the nuclei and ethidium homodimer-1 to identify membrane-compromised (dead) cells. We found that the cells' response to PA 10 mM is undiminished even 12 hours after staining. These findings support the development of a viability-normalizing method for storable, cell-based olfactory sensors using engineered, desiccation-tolerant Pv11-Or47a cells.

7:30 - 9:30 PM	Sawyer Key
Award Lectures	

Chair(s): Julie Mennella

7:30 **Achems Young Investigator Awardee**
Kevin Bolding
Monell Chemical Senses Center

8:00 **Lawless Award For Research Excellence In The Psychophysics Of Human Taste And Smell**
Emily Mayhew
Michigan State University

8:30 **Ajinomoto Awardee**
Roberto Vincis
Florida State University

9:00 **Max Mozell Awardee**
Thomas Hummel
Technische Universität Dresden

Saturday, April 25, 2026

7:30 - 9:00 AM	Pavilion/ Pavilion Lawn
Continental Breakfast	

8:00 - 10:00 AM	Pavilion
Poster Session V	

300 **Response Stability Across Standard And Forced-Choice Formats Of The Waterless Empirical Taste Test (Wett)**

Shima T. Moein[1], Ryan Sharetts[1], Ricahrd Doty[1,2]

[1]Research & Development Division, Sensonics International, Haddon Heights, NJ, United States, [2]Smell & Taste Center, Department of Otorhinolaryngology-Head and Neck Surgery, Perelman School of Medicine, University of Pennsylvania, Philadelphi, PA, United States

The Waterless Empirical Taste Test (WETT) includes six response options: sweet, sour, salty, bitter, brothy (umami), and “no taste.” Because excessive endorsement of “no taste” may be used to feign gustatory dysfunction, we examined the effect of removing this option on test performance in healthy individuals and explored implications for detecting atypical responding. Ninety-eight healthy participants (75 women; age range 6–76 years) completed two within-subject administrations of the WETT: (1) standard 6-alternative format and (2) forced 5-alternative format without the “no taste” option. Total and individual taste scores were compared using paired t-tests. Total score was higher in the standard format (34.0 ± 8.9) than in the forced-choice format (25.1 ± 9.0; $t(97)=10.08$, $p<0.001$), reflecting frequent selection of “no taste.” However, when “no taste” responses were subtracted from the standard total, adjusted scores (24.1 ± 7.7) did not differ significantly from forced-choice totals ($p=0.20$). Individual taste scores were largely stable across formats, with only a modest increase in sweet responses under forced choice ($p=0.029$). These findings demonstrate that healthy individuals show consistent performance across formats when scoring is harmonized. We propose that administering both formats may provide a practical approach for evaluating response validity: substantial discrepancies between standard and forced-choice performance could indicate atypical or non-credible responding. Further research in clinical and simulated malingering populations is warranted.

302 **Investigating The Modulation Of Retronasal Smell And Taste Perception By Carbonation Using A Novel Sip Gustometer (Sg).**

Hanzhi Zheng, Tiffany Hsu, Dando Robin, Terry Acree
Cornell University, Ithaca, NY, United States

A recent study using endoscopy showed aerosols generated during the oral processing of liquids, particularly carbonated ones. These flavor-containing liquid droplets when dissolved in the olfactory epithelium were reported to enhance flavor perception. However, other reports indicate that carbonation exerts an inhibitory effect on the brain’s neural processing of flavor perception, and it significantly reduces the neural activity related to sweet taste in key gustatory brain regions with a more pronounced suppressive impact on sucrose than on artificial sweeteners In order to elucidate the modulatory effects of carbonation (possibly caused by aerosols) on flavor perception, this study used a novel gustometer called a Sip Gustometer (SG) that delivers 1ml of a flavored solution to the tip of a subject’s tongue in less than one second. When combined with a Sniff Olfactometer (SO) both controlled by the same PsychoPy program, we hope to parse the effects of retronasal odor detection on the taste perception of carbonated beverages. In the preliminary experiment reported here, we measured the effects of carbonation on the retronasal response to ethyl butyrate odor, an apple-like odorant combined with sucrose and with or without carbonation. A logistic dose-response model was computed using a two alternate forced choice paradigm (“apple smell” or “no apple smell”) in carbonated and non-carbonated water as comparative conditions, and each target sample was prepared at six concentrations from below the threshold to above and tested 6 times. The results from four subjects are precise enough to quantify carbonation’s effects on retronasal aroma and distinguish differences among subjects.

304 **Exploring The Link Between Oral Sensitivity And Mealtime Challenges In Picky Eaters**

Berenice I. Montano Rodriguez, Christopher T. Simons
The Ohio State University, Columbus, OH, United States

Picky eating in children can lead to mealtime stress and poor nutrition and may be influenced by heightened oral sensitivity and parental perceptions. Therefore, we assessed oral tactile and taste sensitivity and parental perceptions of eating behavior in picky (PE) (N=17) and non-picky eaters (N=52) aged 8-17 yrs. We hypothesized that PE would exhibit greater sensory sensitivity, lower dietary diversity, and more adverse mealtime behaviors. Children were classified as picky using the “Fussiness” and “Enjoyment of Food” sections of the Development Children's Eating Behavior Questionnaire and a parent screener reporting ≥2 instances

where the child “never,” “almost never,” or “sometimes” (a) ate the same food as the family, (b) consumed fruits and vegetables, or (c) ate an adequate amount of food during meals. Just-noticeable difference (JND) thresholds for punctate pressure, roughness, viscosity, and bitterness were assessed using aesthesiometers, graduated metal coupons, xanthan gum, and quinine solutions, respectively. Dietary diversity and mealtime behaviors were evaluated using the Children’s Dietary Questionnaire and the Mealtime Behavior Questionnaire. Group differences were analyzed using unpaired *t*-tests ($\alpha = 0.05$). No significant differences between group group tactile or taste JNDs were found although punctate pressure showed a marginal effect favoring greater sensitivity in PE. Additionally, PE showed poorer diet diversity (p=0.0019) and fruit and vegetable intake (p=0.00259), more adverse mealtime behaviors with higher food refusal (p=0.00149) and mealtime aggression (p=0.0163). While no significant differences were found in tactile or taste thresholds, a small effect for roughness detection suggests that oral texture perception may warrant further exploration.

306 **Evidence For Modulation Of The Sour Taste Receptor Otop1 By Compounds Associated With Licorice Aftertaste**

sabrina Corazza, Manuel Arcangeletti, Irene Riva, Menella Valotta, Katja Blasi, Marcel Winnig, Jean-Francois Rolland
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OTOP1 is a proton-selective ion channel expressed in taste receptor cells and has been identified as a critical molecular sensor for sour taste (Tu et al., 2018; Sladkov & Kolesnikov, 2024). In addition, OTOP1 has recently been reported to act as a sensor for ammonium chloride (NH_4Cl), a tastant described as bitter, salty, and mildly sour, which is a key component of salty licorice (Zhang et al., 2023). In this study, we developed a reliable high throughput automated electrophysiological assay to investigate OTOP1 function and modulation. Human OTOP1 was transiently expressed in CHO cells using MaxCyte electroporation, and recording conditions were optimized on the SyncroPatch 384 platform to achieve stable and reproducible measurements of proton-mediated currents. We then tested a panel of sweet-tasting compounds, selected based on their association with a licorice-like aftertaste. Several compounds exhibited inhibitory effects on OTOP1-mediated proton currents at the SyncroPatch 384. To validate these findings, three representative compounds (one strongly associated with licorice aftertaste, one showing weaker activity and one negative control) were further examined using the golden standard method for electrophysiology i.e. manual patch-clamp confirming the effects observed in the automated assay. Together, these findings establish a robust assay for studying OTOP1 pharmacology and provide evidence that sweetener-associated compounds can modulate a key taste receptor involved in sour and ammonium taste, offering new insight into molecular mechanisms underlying complex taste perceptions.

308 **Individual Differences In Oral Sensitivity To Sucrose And Dairy Fat**

Victoria Esparza[1], Catherine Peyrot des Gachons[1], Amy Huang [1], Nancy Rawson [1], Paul Breslin [1,2], Linda Flammer [1], Paul Wise [1]
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Individual differences in taste and smell are associated with individual differences in food preference. Variation in sensitivity to mouthfeel has received less attention in this regard, for example mouthfeel sensations from beverages such as perceived “body” or “weight.” Toward addressing this gap, we characterized distributions of sensitivity to the mouthfeel of sucrose (in aqueous solution) and dairy fat (added to a skim milk base) by measuring replicated oral detection thresholds in 58 healthy adults, eliminating visual cues and retro-nasal olfaction. For sucrose stimuli, lactisole was added and participants rinsed with gymnema sylvestre tea to suppress sweetness. Sucrose thresholds varied widely, from 5.2% to greater than 36% w/v, with a median of 22.5% (SD = 11.5%). Thus, with reduced sensory cues most participants failed to detect concentrations in typical sodas (about 10-11% sugar). Dairy fat thresholds also varied widely, from below 0.6% to greater than 20% w/v, with a median of 3.4% (SD = 7.9%). Thus, with reduced sensory cues about half the participants failed to detect dairy fat at concentrations close to that of whole milk (about 3.25 to 3.5% dairy fat). Sucrose and dairy fat thresholds were weakly but significantly correlated, r =0.35, p=0.008, suggesting potential shared sensitivity and detection mechanisms. Taken together, our findings indicate that when sensory cues including sweet taste and retro-nasal olfaction are reduced, many individuals show limited sensitivity to oral sensation from sucrose and dairy fat at beverage-relevant concentrations. Additional research is needed to determine the underlying mechanisms of these individual differences and their role in shaping sugar and fat preferences.

310 **Impact Of Oral Microbiome Perturbation On Orthonasal And Retronasal Olfactory Perception.**

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The olfactory system operates through two distinct pathways: orthonasal and retronasal. Both pathways converge on receptors at the olfactory epithelium, yet perception of a given stimulus is thought to depend on the pathway taken. Emerging evidence suggests that oral microorganisms may alter retronasal aroma perception, contributing to these pathway-dependent differences. Presently, we investigated whether broad reduction of oral microbial load affects perceptual performance across pathways. Thirty participants engaged in a flavor-matching task under baseline and post-microbial-perturbation conditions. Equintense aqueous flavors (rose, jasmine, lavender, and honeysuckle) were delivered per trial as a reference either orthonasally (ON) or retronasally (RN). Participants then selected the matching stimulus from four blinded options, presented either through the same route (congruent: ON-ON, RN-RN) or different route (incongruent: ON-RN, RN-ON). Microbial load was broadly reduced using three 0.25% sodium dodecyl sulfate (SDS) rinses, brushing, and tongue scraping. Unstimulated saliva was collected for CFU/mL quantification. Results indicate the SDS treatment significantly (p<0.001) reduced microbial load by 1.3 log CFU/mL. Despite this, matching performance and signal detection measures

indicated that performance did not differ between control and SDS conditions. Consistent with prior studies, performance remained superior in congruent trials, further confirming route-dependent differences. The minimal effect of SDS suggests that this level of microbial reduction may be inadequate to shift perception; greater or more targeted microbial or metabolic perturbation may be needed to isolate microbial contributions to sensory perception.

312 **Intensity Alters Identity: Odor Quality Shifts Across Concentration**

Aurora E. Anderson[1,2], Elizabeth A. Hamel[1], Xuebo Song[1], Christiane Danilo[1], Robert Pellegrino[1], Joel D. Mainland[1]

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Although most odor atlases describe the odor character of a given molecule using a single description, odor character can change across intensities. Other sensory modalities have similar phenomena, for example the Bezold-Brucke effect in color vision where hue varies with luminescence and the Zurmuhl-Stevens effect in audition, where perceived pitch varies with sound pressure. Previous work established that odor quality differs at low and high intensities, but modeling how and where this shift occurs has remained unclear. To address this gap, we asked 15 trained participants to rate the applicability of 51 odor descriptors of 25 odorants. Each odorant was tested at 6 intensities chosen to span from low to high perceived intensity, allowing odor quality to be modeled as a continuous function of concentration. For 16% of odorants, variation within a molecule exceeded typical character differences seen between molecules (mean cosine distance = 1.14). This variability indicates that individual odorants can evoke a richer range of percepts by occupying different regions of descriptor space across intensities. Developing a predictive framework for this diversity of character expands our ability to manipulate, reformulate, and generate desired odor qualities.

314 **Subjective And Objective Measures Of Olfaction In Pregnancy**

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Most pregnant women report a heightened sense of smell, but superior performance on standard objective measures of olfaction has rarely been reported. In this study, differences in odor perception between pregnant and non-pregnant women, using several subjective and objective tests, were explored. Twenty pregnant and 20 non-pregnant women completed a survey that included rating their sense of smell and reporting symptoms of nausea and vomiting using the Pregnancy-Unique Quantification of Emesis (PUQE) questionnaire. Pregnant women were also asked to identify odors to which they were more sensitive. All participants completed 3 olfaction tasks: a novel 22-trial odor discrimination task using the triangle method with primarily common food items; a 22-odor naming and rating task, and an amyl acetate odor detection task using the method of constant stimuli. There was no significant difference between non-pregnant and pregnant women's pre-pregnancy ratings of sense of smell, but pregnant women rated their sense of smell significantly higher than before pregnancy and than non-pregnant controls. Moreover, 95% of pregnant women identified specific odors to which they were more sensitive and their PUQE scores were significantly higher than controls. However, pregnant women did not differ from controls in their odor discrimination performance (overall performance was ~78%), nor in their ability to detect amyl acetate (overall performance was ~ 68%). There were no differences between groups in average ratings of odor intensity, familiarity nor pleasantness and pregnant women were no better at naming odors. The results of this study highlight the questionable relationship between subjective and objective measures of olfaction and leave open the question: What changes in odor perception during pregnancy?

316 **Neural Representations And Task Design In Clinical Olfactory Testing**

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Olfactory dysfunction is common and clinically significant, yet objective assessment of human smell function remains limited. Clinical assays, such as the Threshold, Discrimination, and Identification (TDI) tests, are grounded in classical psychophysics but differ substantially in task structure, decision-making criteria, and cognitive demands. We modeled odor-concentration pairs as vectors in an odor representational space with variability and vector lengths scaling with response magnitude, inspired by neural population codes. Behavioral tasks were simulated as forced-choice decisions over noisy clouds of points corresponding to background and odor-evoked representations. Performance was quantified using signal detection theory and classification accuracy from linear discriminant analysis.
Simulations showed that improved performance with increasing stimulus intensity arises from increased separability of neural patterns relative to noise. Discrimination performance depended on task format: performance of the tasks comparing two stimuli was better when odors were highly overlapping, whereas performance of the tasks involving three stimuli became better once one odor clearly stood apart from the others. Identification efficiency was impaired when representations were highly similar, reflecting competition among multiple possible matches, but outperformed discrimination once odors were well separated. TDI tasks differed in difficulty not only due to the number of alternatives, but also because they impose distinct comparison operations and decision bounds. Our framework helps explain how differences in task structure and noise may contribute to divergent outcomes across olfactory assays and may offer guidance for the interpretation and design of clinical smell tests.

318 **Discrimination Of Viral And Non-Viral Cells Through Volatile Organic Compound Profiling Of Culture-Derived Headspace**

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The highly advanced canine olfactory system is utilized across fields of odor detection, with recently emerging applications in biological threats and disease surveillance. Selection of training materials is critical for optimal discriminatory performance, where target odors must be representative of the true material and distractor odors must be contextually relevant. Due to the metabolic complexity and unknown odor profiles of most biomaterials, it is challenging to include distinct yet operationally relevant distractors. To understand odor-based discrimination and optimize the application of non-invasive chemosensory detection of infectious agents, we chemically characterized the volatile organic compound (VOC) profiles of two separate cell culture models (Channel Catfish Oocytes-CCO and Madin-Darby Bovine Kidney-MDBK) under eustress and stress conditions through induction of viral infection, thermal stress and/or cellular crowding. Viral targets included Channel Catfish Virus (CCV) and Bovine Viral Diarrhea Virus (BVDV). The viral distractor included Bovine Herpes Virus (BoHV) and non-viral groups included cell-free growth media, healthy cells and/or or alternatively stressed cells through thermal or overcrowding conditions. Real-time headspace analysis using Proton Transfer Reaction-Mass Spectrometry (PTR-MS) demonstrated distinguishable odor signatures for each viral model compared to non-infected controls, as well as shared features across different forms of physiological stress. These results contribute to understanding the volatile signature of viral cell culture models of interest while highlighting the importance of intentional distractor odor selection in canine training to meet the challenge and complexity of biological targets.

320 **Smelling Diseases: Olfactory Ai For Early Diagnosis**

Ichie Ojiro[1], Vivek Agarwal [2], Rory Reiser[1], Dina Popova[1], Idan Frumin[1], Vasant Dhar[2], Bruce Kimball[3], Dmitry Rinberg[1]

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We developed a new diagnostic platform integrates the sensitivity of the mouse olfactory system with artificial intelligence to extract disease-specific odor profiles ("*odorprints*") from biological fluids. Accumulating evidence indicates that a wide range of diseases, such as diabetes and infections, alter the odor of biological fluids, including urine, blood and breath, generating disease-specific *odorprints* with strong potential as diagnostic markers. However, biological fluids are influenced by individual background factors, such as diet, age and environment, making it difficult to isolate disease-specific *odorprint*s signatures chemically. Surprisingly, animals can robustly detect and discriminate these disease-specific *odorprints*. Despite this capability, labor-intensive behavioral training makes clinical application difficult, and incomplete understanding of olfactory mechanisms has hindered development of artificial system. To develop a system diagnoses disease directly from odor-evoked neural activity in the olfactory bulb, we combined high-sensitivity *in vivo* imaging of olfactory neural activity with machine learning to extract disease-specific *odorprint* signals. To test our concept, an inflammatory disease model was established by injecting mice with lipopolysaccharide (LPS). Urine samples collected before and after injection were presented to GCaMP-expressing OMP mice, and glomerular responses were recorded. The data were used to train the model, which successfully discriminated LPS/non-LPS samples. These results demonstrate that disease-specific *odorprints* are decodable from olfactory neural activity using machine learning, providing a foundation for rapid odor-based screening tools and advancing our understanding of how the olfactory system processes complex biological mixtures.

322 **Olfactory Detection Thresholds Of Mice To Commonly Used Odorants**

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Perceptual measures of olfactory sensitivity reflect the responses derived from the complete repertoire of olfactory receptors and therefore provide a mechanism to compare the sensitivity of different species, gauge appropriate stimulus concentrations for functional experiments, and develop hypotheses regarding the evolutionary pressures that have shaped the olfactory receptor gene repertoire. In this study, we assayed the ability of C57Bl/6J mice to detect six odorants: sec-butyl acetate, isobutanol, benzaldehyde, 2-butanone, 2-pentanone, and 2-hexanone using our robust psychophysical approach combined with a photoionization detector method to validate vapor-phase concentration. We found that mice were most sensitive to sec-butyl acetate (15.5 ppb) and benzaldehyde (16.6 ppb) and least sensitive to the three ketones (2-butanone: 161.2 ppb, 2-pentanone: 112.9 ppb, and 2-hexanone: 122.3 ppb). Integrating these new findings with our previously published data, we find that murine olfactory thresholds (n = 29 odorants) range across four orders of magnitude (0.1 – 250 ppb). In general, mice exhibited the greatest sensitivity towards aliphatic alcohols and the least sensitivity towards ketones. We hypothesize that enhanced sensitivity towards alcohols could potentially assist in the identification of spoiled grains, which is a major food source for both wild and laboratory mice. Beyond aiding researchers in using appropriate stimulus concentrations for functional studies in mice, these sensitivity measures can shed light onto the evolutionary pressures that have shaped their olfactory system.

324 **Vector-Based Taste Representations Of Food Odours Predict Appetitive Value**

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Flavour perception arises from the integration of gustatory and olfactory signals, yet how learned taste-odour associations are represented in the brain and translated into appetitive behaviour remains poorly understood. Our prior work demonstrated that aromas acquire taste-like neural representations through flavour learning: using a flavour-binding paradigm and fMRI, we showed that tasteless aromas evoke activity patterns in the human insular cortex that overlap with those elicited by their paired tastants, particularly in the dysgranular and agranular insula. These findings established a shared and dynamic neural code for taste and retronasal olfaction, providing a cortical mechanism through which aromas acquire consummatory meaning. Building on this neural framework, the present pre-registered study extends taste-odour integration beyond retronasal perception to orthonasal food odours and examines how predicted taste properties modulate food wanting. Healthy volunteers completed a taste-rating session to derive individual sweet and savoury preference, followed by ratings of orthonasally delivered food odours along sweetness, savouriness and wanting dimensions. Mixed-effects modelling predicted odour-elicited food wanting from an interaction between individual taste liking and the expected taste properties of food odours. Moreover, a vector-based representation of odours in sweet-savoury space outperformed a scalar spectral model in predicting appetitiveness, with cross-validated generalisation across participants. Together, these findings link shared taste-odour neural coding in the insula to orthonasal odour-guided appetitive behaviour, highlighting how lifelong associative learning shapes food valuation and suggesting mechanisms through which sensory expectations influence dietary choices.

326 **Odor Concentration Shapes Odor-Taste Mixture Preference And Retronasal Detection In Rats**

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Human psychophysical studies demonstrate fundamental interactions between odors and tastes that give rise to flavor perception, with odor concentration modulating perceived intensity and pleasantness and enabling detection of otherwise subthreshold components. However, in rodents, it remains unclear how odor concentration influences odor-taste mixture preference or what perceptual limits constrain retronasal odor detection. To address this, we conducted two behavioral experiments. First, we used a two-bottle brief-access task in female rats to assess preference among odor-taste mixtures in which taste concentration was held constant (0.1 M sucrose) while odor concentration varied (0.001%, 0.01%, 0.1%). Rats consistently preferred mixtures containing lower odor concentrations, indicating that odor concentration systematically influences consummatory choice in odor-taste mixtures. Because odors in orally consumed mixtures are sampled retronasally, defining retronasal perceptual limits is crucial for understanding multisensory influences on mixture preference. We assessed retronasal odor detection using a modified two-response operant task. Rats discriminated water from odorized-water sampled from a vacuum-surrounded spout designed to minimize orthonasal contamination. Performance was measured across descending odor concentrations until accuracy declined to chance. Preliminary psychometric functions indicate that retronasal detection thresholds occur at higher nominal concentrations than those reported for orthonasal detection, reflecting differences in stimulus phase and volatilization. Together, these experiments demonstrate that odor concentration modulates odor-taste mixture preference and establish retronasal detection thresholds that shape how odor influences consummatory behavior.

328 **Assessing Olfactory Modulation Of Visual Stimulus Processing As A Function Of Trait Anxiety**

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Brain imaging studies demonstrate the ability of odors to modulate neural responses to emotional visual cues, an effect that appears to be further influenced by individual differences in stress and anxiety. Converging lines of evidence indicate that anxious children and adults have a particularly heightened sensitivity to the smoke-like odor of guaiacol (GUA). The current study utilized scalp-recorded electroencephalogram (EEG)-derived late positive potential (LPP) to assess odor modulation of pleasant, unpleasant, and neutral faces and scenes. Ten (6F/4M), normosmic ($TDI_{M\pm SD}$=32.8±4.5), adults ($age_{M\pm SD}$=45.3±10.1) were fitted with a 32-channel EEG system and underwent 2 trials of emotional stimulus processing. Trials consisted of 36 odor-picture blocks with images of pleasant, neutral, and unpleasant faces or scenes (counterbalanced by trial) and odors of GUA, phenyl ethyl alcohol (PEA), and odorless air, with each odor-image type paired 4 times. Consistent with previous studies on emotional visual processing, the mean amplitude of the LPP during the odorless condition was significantly elevated in response to unpleasant, compared to neutral and pleasant, images ($F(2,32)=3.62$, $p=.041$). When participants were grouped by low (n=5, M±SD=26.4±2.9) and elevated (n=5, M±SD=40.0±7.8) trait anxiety, a significant image x odor x trait anxiety interaction was noted ($F(2,32)=4.63$, $p=.017$). GUA, but not PEA, increased the mean LPP amplitude in response to pleasant images in only those with elevated anxiety, reaching a level comparable to that elicited by the unpleasant images during the odorless control condition. These findings expand upon previous work highlighting the top-down role of trait anxiety, in combination with olfactory processing, to influence the visual perception of emotional stimuli.

330 **Cultural Evolution In Perfumes Since 1900**

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Perfume is a cultural artifact shaped by sociocultural norms, stylistic innovation, and collaborative networks. Using a dataset of over 92,000 commercial fragrances released between the late 19th century and 2024, we explore the long-term dynamics of perfumery and scent design. We identify three epochs in perfumery; the Classic Perfumery Era, the Stagnation Era, and the Industrial Perfumery Era, each characterized by distinct shifts in growth, compositional complexity, and innovation. We examine how classical perfume metrics, such as longevity, sillage, and price, have evolved over time, alongside broader industry shifts such as the rise of unisex fragrances and the expansion of the perfumer's palette through synthetic ingredients. Our analysis reveals high levels of homophily in the network of perfume collaborations suggesting that scent design is often driven by perfumers using a similar style. Our findings position perfume as a culturally evolving system, akin to music and fashion, through which societies express, communicate, and iterate aesthetic values.

332 **Valence-Dependent Modulation Of Sniff Volume Is Sustained Across Sniffs**

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Multiple studies have demonstrated that sniff parameters are modulated by an odor's perceived valence in that negative odors trigger a smaller sniff. The robustness of this valence-related modulation is underscored by its use as the basis for a clinical assessment of olfactory dysfunction, known as the Sniff magnitude test. To date, however, valence-dependent modulation has only been demonstrated for the initial sniff of an odor; whether similar effects extend to subsequent sniffs during continued odor exposure remains unknown. Participants (n=41) smelled 4 iso-intense odors (2 clearly pleasant, 2 clearly unpleasant) presented in jars, 3 times of the same ongoing odor, while their nasal airflow was assessed using a spirometer with nasal canula. Valence ratings were obtained for all sniffs, and individual ratings were used for subsequent analyses. Each odor was presented a total of 15 times. Skin conductance served as a distractor to mask the focus on respiration and ensure natural sniffing behavior. As expected, negative odors produced lower sniff volumes, when compared to positive odors, for the first sniff ($p<.001$). The clear difference in sniff volumes between valences was sustained for the two following sniffs (both $p<.001$). Interestingly, contrary to previous reports, this was not a universal effect. 46% of participants did not have a significant valence-dependent modulation of their sniff response. In conclusion, we can replicate and extend effects of valence-dependent sniff modulation also for subsequent sniffs, but the individual differences bring the usability of the previously proposed sniff magnitude test into question.

334 **From Roses To Rubbish: Toward A Standardized Children&Rsquo;S Lexicon Of Odor Sources**

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The odors listed spontaneously by adults can be categorized into food & drink, nature, civilization, and social relationships areas, reflecting culturally shared semantic structures and learned environmental regularities. Adult olfactory representations are shaped by experience, language, and functional relevance. Yet, it is still unclear how children describe their olfactory surroundings and whether they categorize them similarly to adults. To this end, we performed a qualitative analysis on the odor sources that are listed by children in a free listing task. A total of 151 children aged 3-9 years (*Mage*=6.52±1.19 years; 74 girls) participated in the study. Children named as many odors as possible from their daily environment without time constraints. Responses were standardized using a lemmatization approach, performed independently by two experts, followed by a consensus discussion. Resulting lemmas were categorized according to odor sources, contextual references, and affective descriptors. The final dataset comprised 404 odor sources. The most frequently mentioned were *flower* (*n*=64), followed by *food* (*n*=42), *tree* (*n*=39), and *leaf* (*n*=32). In addition, 153 distinct contextual references were identified, with the most frequent being *forest* (*n*=26), *kitchen* (*n*=13), *kindergarten* (*n*=11), and *wet* (*n*=11). Children also listed 26 unique descriptors, including *fresh* (*n*=13), *smelly* (*n*=5), *nice* (*n*=4), *old* (*n*=4), and *sweaty* (*n*=4). These findings indicate that children's spontaneous representations of odors are grounded in concrete, everyday environmental and food-related sources, reflecting primary functions of olfaction. The results provide a structured lexical foundation for understanding early olfactory representations and may inform the development of age-appropriate odor identification and naming tools.

336 **Fair Chemosensory Data: Unlocking Ai For Flavor, Food And Health**

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Background: Chemosensory perception is a major driver of food choice, intake, product acceptance and health, yet sensory data in this domain remain fragmented, inconsistently reported and rarely shared in machine-readable form. This limits cumulative progress and prevents the development of robust AI models that could transform food innovation, personalized nutrition and clinical chemosensory applications. Methods: By synthesizing lessons from data-intensive fields and mapping them onto current chemosensory infrastructures, including existing databases such as FoodOn, BitterDB, FlavorDB, Pyrfume and Hub4Smell, we frame these efforts within the Findable, Accessible, Interoperable and Reusable (FAIR) principles and identify minimal, high-impact actions towards changing this situation. One actionable item is to share one's available data in the ChemoSensory Data community (https://zenodo.org/communities/chemosensorydata/). Results: Concrete steps by researchers, editors, funders, societies and software vendors can contribute towards chemosensory data FAIRness. These include publishing tidy sensory tables with core metadata, adopting shared ontologies and common data elements, implementing standardized export formats in sensory software, and exploring federated learning options to leverage industrial datasets without exposing confidential information. Conclusion: Making chemosensory data FAIR is both feasible and urgently needed to unlock AI for chemosensory science and health. Coordinated but incremental adoption of shared standards, repositories and privacy-preserving collaborations will enable interoperable chemosensory datasets that support predictive modeling, cross-sector innovation and more equitable access to chemosensory insights worldwide.

340 **Biologically Informed Artificial Intelligence Models For Predicting Human Sensory Perception Of Scents And Flavours**

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Human sensory perception is shaped by scent and flavor intensity, a key driver of consumer acceptance. Predicting olfactory intensity is a central challenge; traditional sensory panels are reliable but expensive and difficult to scale. Furthermore, the industry faces a loss of tacit expertise as experienced perfumers retire. While computational models offer scalability, they often lack biological plausibility and fail to capture the nonlinear, compound-specific dose–response behavior governing intensity. These gaps stem from scarce datasets and the difficulty of modeling complex psychophysical relationships. To overcome this, we introduce a biologically informed machine learning framework that integrates psychophysical principles into the learning process. The model embeds Hill's law to constrain predictions to realistic dose–response behavior, preventing the unrealistic linear growth of conventional models. We set the minimum perceived intensity to 1.4 and estimate maximum concentration via log vapor pressure, sampling dose–response curves at ten points. These representations are coupled with Graph Neural Networks (GNNs) using molecular graphs to link chemical structure to perceptual outcomes. Validation in the perfume domain showed that embedding odor-character representations within the intensity prediction pipeline reduced mean squared error by approximately 20% compared to structure-only baselines. This study demonstrates that embedding principles like Hill's law into AI enhances predictive power and interpretability, offering a tool for rational fragrance design that reduces reliance on costly sensory panels.

342 **Developing And Validating A Quest-Based Method To Measure Odor Detection Thresholds**

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Odor detection thresholds vary substantially across individuals, and they decline with age and in some disease states. Thus, accurate and efficient methods for quantifying these thresholds are essential. Currently, the staircase algorithm is applied almost universally to navigate stimulus intensity steps in odor detection threshold tasks, but the QUEST algorithm could be a more flexible and efficient alternative. QUEST is routinely implemented to measure detection thresholds in the visual domain, but there are only two studies along these lines in the olfactory domain, both of which utilize odorized pens for stimulus delivery. Here, we develop and validate a QUEST-based method to measure odor detection thresholds with a computer-controlled olfactometer. More specifically, participants (n = 54) strived to detect a weak odor (n-butanol) among odorless foils in a 3-alternative forced choice task, where QUEST directed the stimulus intensity trajectory to be maximally informative. Next, participants completed a similar odor detection task based on the more established method of constant stimuli. We found that the QUEST approach yields a threshold output that is highly comparable to that from the method of constant stimuli, despite requiring far fewer trials. This suggests that the method is an accurate and expedient tool, which could be leveraged in olfactory research and clinical settings.

344 **Does The Nasal Cycle Provide An Attentional Gain In Olfaction**

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Nasal airflow is asymmetric across nostrils, greater in one nostril over the other. This asymmetry fluctuates on an ultradian cycle known as the nasal cycle. Whereas the offset across nostrils increases the range of molecules within optimal sensitivity, why this offset shifts over time, and the relevance of this shift to olfaction, remain unknown. Here we hypothesized that this shift may provide for attentional gain. More specifically, we hypothesized that when asymmetry is reduced, the measure of central noise is reduced, and therefore sensitivity will be higher. To test this hypothesis, we sat participants to watch a monotonic nature film in a room, while 6 odorant events, each lasting 10 seconds, were generated in the ambient air once about every 7 minutes. A combination of photo-ionization detector and electronic nose were used to sample the air directly above the nose, so as to gain a measure of odor dispersion. Participants were instructed to press a button at any time during the 45-minute experiment if they experienced a change in ambient smell. Nostril-specific nasal airflow was measured concurrently. To date, we studied 19 participants (11F) using two sets of 6 odorants (15 participants set #1, 4 participants set #2). Mean F1 score was 0.51 (SD = 0.15), implying that we were within psychophysical range. However, we failed to observe any relation between the nasal cycle and either accuracy (r = 0.1) or reaction time (r = 0.14). In turn, in-depth analysis revealed that in the 4 participants using the second odorant set, accuracy consistently shifted with asymmetry. These merits matching cohort size, and the complete investigation of this pattern will be presented.

346 **A Human-Nose-Inspired Biomimetic Electronic Nose**

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Electronic noses (eNoses) have been used in a variety of applications from detection and classification of odorants to predicting their perceptual semantic descriptions. Extensive efforts have been directed at sensor technology, but despite their names, the design and function of electronic noses has little to do with that of the biological system. We built a human-nose–inspired biomimetic eNose to test the functional value of specific nasal features and sampling strategies. Using high-resolution 3D printing, we reproduced a CT-derived model of a human female nasal cavity. Mass-flow controllers (MKS) at the pharynx generated realistic breathing waveforms, and sensors were positioned at the olfactory cleft—the native location of the olfactory epithelium. The platform can host diverse sensing technologies; here we first tested two Airsense PEN 3 units (metal-oxide array, 10 coatings each), one per nostril, set to sample at 10Hz. To mimic realistic sampling, odors were not provided by olfactometer or autosampler, but were rather sniffed from wide-mouth jars, mimicking a typical human olfactory experience. In an initial experiment we asked whether olfaction benefits from treating the previous inhalation as a running, dynamic baseline. We classified naturalistic odorants drawn from a list of the most commonly encountered smells (e.g., pine needles, fresh fruit, chocolate, peanut butter). Implementing a running baseline improved classification accuracy by 45% ($p < 0.0001$). This result suggests a practical strategy for coping with dynamic odor environments that immediately boosted eNose performance. Additional biomimetic manipulations will be presented.

348
11:15 **Scaling Sensory Annotation Of Odor Mixtures With A Prior-Guided Sensory Annotation Tool**

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Data-driven approaches to olfactory prediction require large volumes of high-quality, consistent sensory annotations—particularly for odor mixtures, which dominate real-world olfactory experiences but remain challenging to characterize at scale. At Osmo, we have built *Studio*, a caption-to-mixture platform for fragrance creation. A critical prerequisite for this effort is the ability to efficiently and reliably annotate complex odor mixtures within a shared, scalable taxonomy of olfactory terms. Traditional sensory annotation of mixtures is limited by low throughput, annotator variability, and cognitive load, especially when mixtures evoke overlapping or ambiguous perceptual qualities. To address these challenges, we developed a novel annotation tool designed to scale taxonomy-based mixture annotation while maintaining data quality and internal consistency. This tool introduces a structured annotation workflow supported by a probabilistic prior derived from a linear mixture model of odor components – using previous annotations or model predictions for each component – building on prior work in mixture perception and representation. This prior provides an initial hypothesis for mixture descriptors, which annotators can then refine based on perceptual experience. We describe the design of this new tool, the process by which priors are generated, and key tradeoffs of the approach including gains in annotation throughput and consistency, potential biases introduced by model-informed priors, and the extent to which human annotators can correct inaccurate priors. Together, these findings highlight a practical path toward collecting large-scale, high-quality mixture annotations to support the next generation of data-driven fragrance creation tools.

350 **High-Resolution Optical Imaging Distinguishes Olfactory And Respiratory Epithelium In Mouse And Human Nasal Tissue**

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Olfactory dysfunction affects up to 10% of the population and is associated with reduced quality of life and early

cognitive decline, yet visualization of the intact olfactory epithelium (OE) in human subjects has been elusive. Current diagnostic and prognostic assessment for smell loss, as well as research methodology, rely on psychophysical testing or small epithelial biopsies that sample only limited regions of the nasal mucosa without ability to reliably obtain OE as opposed to adjacent areas of respiratory epithelium. A minimally invasive method for identifying and assessing the extent of OE within the nasal cavity would provide a major advancement in studying human olfactory disorders. Here, we demonstrate that dynamic micro-optical coherence tomography (dμOCT) can be used as a label-free approach for high-resolution assessment of the OE ex vivo on mouse and human olfactory tissue. Using transgenic mouse tissue to provide a gold standard reference, we identify clear boundaries between olfactory and respiratory epithelium. We then demonstrate using live human explant tissue the ability of dμOCT to not only distinguish between olfactory and respiratory epithelium but also resolve olfactory sensory neurons and duct/gland units. These findings demonstrate that dμOCT can provide reliable identification of OE in vivo. This approach establishes the proof of concept for using dμOCT as an in situ, minimally invasive tool to map human olfactory mucosa, improve biopsy targeting, and enable objective, quantifiable longitudinal assessment of olfactory epithelial health in disease and during recovery.

352 **Odor Aging Induced By Atmospheric Oxidation In A Flow-Tube Reactor**

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The goal of this study on odor aging induced by atmospheric oxidation in a flow reactor is to investigate how odor quality changes due to atmospheric oxidants such as ozone. The study also aims to identify any common features among the oxidized odors from different starting reagent, even if their chemical compositions differ. In this study, TD-GC-Q-TOF was used for chemical characterization, and sensory evaluation, including hedonic ratings as well as odor quality assessments, will be conducted to investigate the relationship between chemical composition and human perception. For ozone oxidation of chemical compounds, a flow reactor was employed to provide a well-defined residence time while minimizing side reactions compared to a chamber system. The system was designed for cartridge sampling followed by TD-GC-Q-TOF qualitative analysis of oxidation products and human perception tests, and the homogeneity at the inlet and outlet of the flow reactor was confirmed. The oxidation of (+)-limonene yielded compounds such as 4-acetyl-1-methylcyclohexene, trans-dihydrocarvone, and carvone. In the perception test conducted with five panelists, three of them described the resulting odor as having changed to a minty or fresh character. So far, oxidation experiments were conducted for (–)-limonene (terpene), α-pinene (herbal), geraniol (floral), cis-3-hexen-1-ol (green), linalool (floral), 1-octen-3-ol (earthy), cinnamyl alcohol (balsamic), anethole (licorice), allyl phenylacetate (honey), and ocimenes (floral), and only qualitative analyses were performed. Further perception tests will be conducted using a triangle test method, and hedonic reports as well as an inspiratory volume sensor will be incorporated into the evaluation criteria.

354 **Hub4Smell: Unifying Fragmented Olfactory Data To Unlock Clinical And Research Insights**

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Background: Olfactory research remains fragmented across disparate sources with little standardization, hindering data aggregation and limiting the translation of olfactory dysfunction findings into clinical applications and innovations. Hub4Smell digital platform (with free and paid services) is an innovation that unifies fragmented olfactory research data into a standardized, FAIR-compliant resource. It consolidates historical datasets, incorporates prospective data, and systematically discovers and curates publicly available olfactory datasets. Methods: We searched available repositories (e.g. PubMed, Zenodo, Figshare, GitHub, OSF) using 25+ domain-specific terms with filters to exclude irrelevant datasets (e.g. non-human, in vitro). To date, we identified 71 datasets evaluated for participant demographics, test type, licensing (e.g., CC BY 4.0, open access, restricted, proprietary), and data quality. Results: Across 71 publicly accessible olfactory datasets evaluated to date, we identified smell test data for 1.5M+ participants, 80+ countries. Notably, 80% of these datasets are licensed for commercial use. Hub4Smell's data curation enables harmonization across heterogeneous databases, allowing a proprietary AI-driven conversational analytics module to run queries across aggregated data, facilitating comparative analyses that were previously invisible within isolated silos. Conclusion: By discovering, standardizing, and integrating existing and prospective olfactory datasets following FAIR principles, Hub4Smell platform transforms fragmented human smell test data into a scalable, accessible resource enabling population-level olfactory phenotyping across geographies and times. This positions olfactory assessment as a standardized biomarker for precision medicine and population health surveillance.

356 **Odor-Induced Taste Enhancement In Healthy Children And Adults**

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Flavor perception arises from central multisensory integration, primarily involving taste and retronasal olfaction. The addition of odorants to foods or beverages can enhance perceived taste intensity, a phenomenon known as odor-induced taste enhancement (OITE). While adult studies suggest that OITE largely reflects associative learning between taste and odor cues, potential developmental differences in this process remain poorly understood. Using secondary analyses of laboratory studies comparing healthy individuals with clinical populations reporting chemosensory dysfunction, we examined OITE across age groups within the healthy cohort. Participants included individuals aged 12–20 years (mean (SD): 17.7 (3.0); 13 females), 21–40 years (26.4 (6.2); 20 females), and 41–80 years (58.8 (11.5); 13 females). Taste and odor intensity were assessed using

the general Labeled Magnitude Scale for stimuli including sucrose with strawberry extract and citric acid with lemon extract, each presented at two concentrations. Participants rated perceived intensity with and without nose clips to isolate retronasal olfactory contributions. ANOVA results indicated that the two older age groups exhibited significantly greater retronasal OITE than the 12–20-year-old group. These findings suggest age-related differences in OITE magnitude. Future studies incorporating pre-test associative training between taste and odor cues are needed to determine whether reduced OITE in younger participants reflects developmental limitations in associative learning or simply reduced experiential exposure.

358 **Quantifying A Novel Rebaudioside M–Brazzein Sweetness Synergy Using Isobole Methods**

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Alternative sweeteners have long been relied on to reduce consumption of added sugars in foods and beverages. The growing demand for sugar reduction has intensified interest in combining high-potency sweeteners to achieve optimized sweetness quality. This study investigated the interaction between rebaudioside M (Reb M), a component of the stevia plant, and the sweet protein brazzein using quantitative isobole analysis to determine whether their combined sweetness response was synergistic, additive, or antagonistic. Aqueous solutions of 70% brazzein and 50% brazzein were made in combination with Reb M across a range of sucrose equivalents. Psychometric dose–response functions for each sweetener were established using a trained sensory panel, followed by evaluation of fixed-ratio mixtures across a range of concentrations. Interaction indices (*I-values*) were calculated. *I-values* were significantly less than 1, indicating synergy between Reb M and brazzein. *I-values* for the 50% brazzein mixtures showed higher synergy than the 70% brazzein mixtures. These findings indicate that Reb M and brazzein act synergistically to produce higher sweetness potency and improved sensory quality, supporting their use in optimized sugar-reduction formulation frameworks.

360 **Trends In Taste And Smell Alterations In The United States: Prevalence And Risk Factors**

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Background: Problems with taste and smell are common, increase with age, and can significantly impair health and quality of life. Methods: Data from the 2024 and 2021 National Health Interview Surveys (NHIS) (N=22,396 and N=20,248, respectively) were used to update estimates and make comparisons with the earlier pre-pandemic National Health and Nutrition Examination Survey (NHANES), 2011-2014, where taste and smell questions were administered to adults aged 40+ years (n=7,413). Prevalence of self-reported smell and taste alterations and disorders were calculated and associations with risk factors, including COVID-19, and access to health care were examined using survey weighted logistic regression, adjusted for socio-demographic characteristics. Results: Prevalence of smell and taste alterations have changed only modestly from prior estimates (23.1% in 2024 vs. 21.8% in 2021 and 22.3% in 2011-14 for smell and 15.0% in 2024 vs. 14.5% in 2021 and 17.8% in 2011-2014 for taste). Trends in smell and taste problems across risk factors were similar between 2024 and 2021. However, problems with smell and taste were more frequently reported among individuals with COVID-19 (52.1% and 42.5%, respectively) in 2021 compared to 2024 (24.4% and 16.1%, respectively), and the odds of a smell or taste problem for individuals with COVID-19 were 4-6 times the odds for individuals without COVID-19 in 2021 but only modestly elevated (25-33%) in 2024. Importantly, individuals who reported seeking health care declined from 2021 to 2024 (16.6% to 13.3% for smell, 24.3% to 19.5% for taste, both $p<0.01$). Conclusions: Smell and taste problems remain prevalent among adults, but a greater understanding of the post-pandemic environment on these disorders may help improve clinical management.

362 **Peripheral Gustatory Degeneration Contributes To Taste Dysfunction In Mouse Models Of Alzheimer&Rsquo;S Disease**

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Malnutrition and weight loss are common comorbidities of Alzheimer’s disease (AD) and are strongly associated with functional decline and increased mortality. Taste dysfunction is frequently reported in AD patients and can precede cognitive symptoms, yet its biological basis remains poorly understood. Most studies have focused on central nervous system degeneration while largely overlooking the potential role of dysfunction peripheral gustatory system. We examined whether AD pathology disrupts peripheral taste structures and their sensory innervation using three neuropathologically distinct mouse models of AD: the 5XFAD amyloid model, the PS19 tauopathy model, and the LOAD2 late-onset AD model, across multiple disease stages. Analysis of fungiform taste buds and geniculate ganglion–derived innervation revealed significantly age- and sex-dependent deficits. In 12-month-old 5XFAD mice, taste bud numbers were reduced in both sexes, whereas taste bud volume loss and reductions in TUJ1+ and PHOX2B+ innervation were observed only in females. In the PS19 model, no changes were detected at 6 months of age. At 9 months, however, PHOX2B+ innervation was selectively reduced without

alterations in total innervation or taste bud number. In 12-month-old LOAD2 mice, taste bud number, taste bud volume, and sensory innervation were all significantly reduced. Together, these findings demonstrate that AD is associated with progressive degeneration of peripheral taste buds and their sensory innervation, suggesting that peripheral gustatory dysfunction may contribute to impaired taste perception, appetite dysregulation, and weight loss in AD.

364 **Cyclophosphamide Chemotherapy Produces A Transient Loss Of Taste Bud Innervation In Mice.**

Ryan M Wood, Emily Holder, Ireland Little, Victoria Valtr, Erin L Vasquez, Krystal A Goyins, Eduardo G Kuri, Kevin Connelly, Saima Humayun, Lindsey Macpherson
Univeristy of San Antonio, San Antonio, TX, United States

Taste dysfunction affects more than 17% of adults in the United States and is especially common among chemotherapy patients, with 50–80% reporting partial or complete taste loss. These changes are often persistent and underrecognized, contributing to malnutrition, delayed recovery, and reduced quality of life. Despite this significant clinical burden, effective treatments remain limited due to an incomplete understanding of the underlying mechanisms. Cyclophosphamide (CYP), a widely used alkylating chemotherapeutic, disrupts taste by damaging mature taste receptor cells (TRCs) and their progenitors. However, proper taste perception also depends on intact gustatory nerve fibers that innervate TRCs, and the effects of CYP on these peripheral nerves remain poorly defined. Here, we examine how CYP alters gustatory innervation and neural integrity using immunohistology to quantify structural changes in taste buds and two-photon microscopy to assess morphological alterations in peripheral gustatory fibers. Emerging evidence suggests TNF/TNFR1 signaling regulates neural development and axonal growth through canonical and reverse signaling pathways. Preliminary data demonstrate TNF/TNFR1 expression in taste tissues, leading us to hypothesize that this pathway contributes to chemotherapy- or inflammation-induced taste dysfunction. Defining these mechanisms may identify novel therapeutic targets to restore taste function.

366 **Persistent Severe Acute Respiratory Syndrome Coronavirus 2 Infection And Taste Nerve Degeneration Driven By Impaired Interferon Regulatory Factor 3 Signaling**

Kang-Hoon Kim[1], Emma Larsson[1], Janna Oh[1], Heaven Branch[1], Peihua Jiang[1], Danielle R. Reed[1], Richard Bowen[2], Hong Wang[1]
[1]Monell Chemical Senses Center, Philadelphia, PA, United States, [2]Colorado State University, Fort Collins, CO, United States

Taste loss is prevalent with SARS-CoV-2 infection. While taste function restored quickly in many patients, some experienced sustained taste loss lasting more than several months. To study the underlying mechanism of taste loss, we used transgenic mouse models that express the human angiotensin-converting enzyme 2 (hACE2), the receptor for SARS-CoV-2 in humans. We used SARS-CoV-2 susceptible hACE2 knock-in and mACE2 knockout mice. Our results show that taste tissues can be infected by SARS-CoV-2, and 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 have shown that inborn genetic errors in key antiviral genes are present in human populations and are 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 (5.4-fold, p=0.008), while viral RNAs were cleared from taste tissues of mice with functional IRF3. Furthermore, we observed a significant reduction of taste nerve fibers within taste buds at 7 and 36 dpi in IRF3-knockout mice. Diminished taste nerve innervation may arise, in part, due to SARS-CoV-2–induced complements that promote synaptic elimination in taste buds. This suggests a mechanistic link between IRF3 deficiency and the pathological impairments underlying long-term post-viral taste loss.

368 **Genetic Variation In Sweet Liking Is Amplified By Real-World Food Contexts**

May M. Cheung[1], Janel Clovis[1], Danielle R. Reed[2], Cailu Lin[2], Amy Huang[2], Liang-Dar Hwang[3]
[1]City University of New York, Brooklyn College, Brooklyn, NY, United States, [2]Monell Chemical Senses Center, Philadelphia, PA, United States, [3]The University of Queensland, St. Lucia, Australia

Individual differences in sweet liking are heritable and are influenced by genetic variation. While many single nucleotide polymorphisms (SNPs) have been associated with sweet taste perception, liking/preference, and intake, heterogeneity in the measurement of sweet-related traits makes it difficult to fully understand which aspect of sweetness these SNPs influence. In a preliminary analysis of an ongoing study, we tested the associations between 204 previously identified sweet-related SNPs and three phenotypes: sweet liking assessed using taste tests; sweet food and beverage liking assessed using a questionnaire; and added sugars intake assessed using a food frequency questionnaire. Analyses were conducted in 295 individuals of African (n = 165) and East Asian (n = 130) descent. After adjusting for age and sex as covariates and correcting for multiple comparisons using the false discovery rate (FDR), 37 SNPs were associated with sweet food and beverage liking, 58 with added sugars intake, whereas none were associated with sweet taste liking. Several SNPs located in *TAS1R2* (rs12033832, rs7534618) and *TAS1R3* (rs307355, rs35744813) were associated with both sweet food and beverage liking and added sugars intake (FDR-adjusted $p < 0.05$). These findings suggest that genetic effects on sweet liking are more detectable when sugar is experienced in an appropriate context (i.e., foods or beverages) rather than in isolated taste tests using sugar solutions. In the future, we aim to test these associations separately in individuals of African and East Asian descent to assess whether these associations are ancestry-specific as a step towards offering more precise nutrition advice based on individual taste preferences.

370 **Reduced Sugar Diets Do Not Affect Perceived Sweetness Or Most Liked Sugar Concentration In Model Foods And Beverages**

Paul M Wise, Gary K Beauchamp
Monell Chemical Senses Center, Philadelphia, PA, United States

Would consumers adjust to reduced added sugars in the food supply, blunting the sweet tooth? To help address this question a diet-controlled, double-blind trial was conducted to test the hypothesis that adults who consume a low sugar diet will prefer less sugar in and taste foods/beverages as sweeter than before the low sugar diet. Participants were 83 healthy adults who consumed > 10% of their total energy from added sugars. After a baseline period (usual diet), participants were assigned to one of 3 study arms with all meals provided for 11 weeks. A comparison group ate the average amount of added sugars for people who consume > 10% of their energy from added sugars. The other two groups consumed 70% less added sugars (37% less total sugars) than the comparison group. For one reduced sugar group sweetness was partially replaced with low calorie sweeteners (LCSs). LCSs were not used for the other reduced sugar group. At baseline and the end of each controlled feeding month participants rated liking and sweetness intensity for a model food and beverage ranging from weakly to strongly sweet. After controlled feeding, participants resumed an uncontrolled diet of their choice for 5-12 weeks before returning for follow-up testing. For both sweetness and most liked sugar concentration, baseline scores were subtracted from post-feeding scores. Resulting difference scores for the reduced sugar groups were compared to the comparison group (Mann-Whitney U tests). No significant differences found ($296.5 < U < 421.5$, $p < 0.13$) and most difference scores were close to 0. These results suggest that the sweet tooth may be less malleable than the taste for salt and imply that other strategies besides sensory acclimation may be required to facilitate reduced sugar intake.

372 **Comparing Video-Based Methods For Spout Lick Detection**

Georgia Davis, Mia Fox, John Boughter, Max Fletcher
University of Tennessee Health Science Center , Memphis, TN, United States

Lick-based measures such as lick count, inter-lick interval (ILI), and lick burst structure are widely used to assess stimulus consumption. Traditional lickometers can accurately count licks, but fail to capture the animals' orofacial movements, which can be evaluated as a measure of palatability. To address this limitation, we developed and evaluated video-based models for lick detection, assessing licking and other consummatory behaviors. Ventral-face videos were collected from head-fixed C57BL/6J mice during sucrose and quinine delivery. Videos were analyzed using a custom DeepLabCut model labeling 32 facial features. Spout licks were detected using three approaches: Identifying tongue-tip entries into a defined region of interest (ROI), a random forest classifier (RFC) trained on the mouth and tongue features, and an RFC trained on a reduced, decorrelated feature set of just the top lip and tongue. RFC detection outcomes were sensitive to facial feature selection, valuation of behavioral frames, and selection of lick probability thresholds. RFCs trained on fewer, less-correlated features showed closer agreement with lickometer measures than higher-dimensional models. Identifying licks using an ROI was comparable with other methods, but it works by using spatial recognition rather than feature determination. Results indicated that selecting a global threshold, applied across videos, was less accurate than determining a lick probability threshold per video. Temporal measures, including ILI distributions, were comparable across methods, although lower frame rates caused temporal binning. These results demonstrate that video-based lick detection is a model-dependent measurement and that feature selection, frame rate, and thresholding strategy critically shape lick detection outcomes.

374 **Taste Experience During A Postnatal Sensitive Window Modifies Preference And Response To Novelty**

Michelle Layana, Hillary C Schiff
Division of Biosciences, College of Dentistry, Ohio State University, Columbus, OH, United States

Postnatal refinement of sensory cortical circuits contributes to perception, decision-making, and cognition, and these processes are modulated by sensory experience. We previously reported that taste experience at weaning influences sweet preference and cortical inhibition in gustatory cortex (GC), the primary sensory region for taste (Schiff et al, 2023), consistent with human studies linking early taste experience to persistent effects on taste preference (e.g. Mennella et al, 2011). Here we find that just 4 days of exposure to Ensure (as opposed to 8) is sufficient to enhance sucrose preference tested at P56 compared to mice exposed only to water. Mice received Ensure for 1 hour/day for 4 days at P25-28 (water n=8, Ensure n=11 mice; $F(4,125)=4.53$, $p<0.01$, F-test); the effect remained whether mice were tested under water restriction or sated conditions. Ongoing studies are assessing Ensure exposure from P22-25. Taste preference influences consumption of nourishing food and avoidance of dangerous substances. To avoid danger, rodents display neophobia, characterized by an initial aversion to new substances, which attenuates after repeated exposures. We report that early Ensure exposure (P22-25) accelerates attenuation of neophobia for saccharin when tested at P56 compared to mice exposed only to water. These findings extend the importance of early life taste experience beyond sucrose preference to responses to novel tastes. Ongoing studies will assess the neural circuit mechanisms recruited by early life exposure to Ensure.

376 **Within-Compound Associations Cause Retrospective Revaluation Of Taste Value In Rats**

Griffin J.M. McFarland, Jian-You Lin, Donald B. Katz
Brandeis University, Waltham, MA, United States

Animals learn about the meaning of stimuli through associative learning, which is not limited to currently presented stimuli but can also apply to stimuli experienced previously, in a phenomenon called retrospective revaluation. To examine how the meaning of taste stimuli can be reevaluated retrospectively, I designed a two-stage conditioning procedure, then asked whether the learning that occurred during stage 2 influenced what was

learned during stage 1. During stage 1, rats were presented with NaCl and sucrose solutions, then given an injection of LiCl to produce a mild conditioned taste aversion (CTA) to both tastes. For stage 2, I presented a novel citric acid solution and either the sucrose or salt solution, again followed by a LiCl injection, creating a combined forward and backwards blocking paradigm. The rats were then given salt, sucrose, and citric acid on separate days to measure their taste preferences, which were compared to those of animals that: 1) received saline injections instead of LiCl; 2) did not receive citric acid in stage 2; or 3) received no stage 2 taste presentations, only water. Preliminary results show a trend where the aversive strength of a taste increases after the stage 2 conditioning, even if that taste was not presented in stage 2. This indicates that a within-compound association formed between the tastes presented together in stage 1, which then produced retrospective revaluation of the absent stimulus after stage 2. Notably, the increase in aversiveness indicates that backwards blocking (a more nuanced form of retrospective revaluation, which would have predicted a decrease in aversiveness) did not occur. Thus, while the rats are capable of performing retrospective revaluation on taste stimuli, it is only a simpler and less nuanced form.

378 **Distribution And Function Of Neurons Producing Gastrin-Releasing Peptide In Mouse Gustatory Cortex**

Diana Guarino[1,2], Lindsey Czarnecki[2], John Chen[1,2], Aylar Berenji Kalkhoran[1,2], Olivia Swanson[1,2], Siddarth Swaminathan[1], Arianna Maffei[1,2], Alfredo Fontanini[1,2]

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The gustatory cortex (GC) integrates sensory, limbic, and cognitive information to guide feeding behavior in the context of the homeostatic state of the animal, yet the cellular mechanisms through which GC encodes homeostatic states and regulates consumption remain poorly understood. Gastrin-releasing peptide (GRP) is a neuropeptide known to reduce consumption, but its role within cortical circuits has yet to be examined. Here, we test the central idea that GC contains neurons that produce GRP (GRP+ neurons), and that these neurons are engaged by gustatory stimulation and are capable of controlling consummatory behaviors. We first relied on anatomical methods to quantify GRP+ neurons in the GC of GRP-tdTomato mice and identified their neurotransmitter identity. Patch clamp recordings in slice confirmed that GC GRP+ neurons are predominantly pyramidal neurons. Upon identifying such a population of GC pyramidal neurons, we recorded their responses to various tastants: sucrose, NaCl, citric acid, quinine, Ensure, and water. We found that GRP+ neurons show taste-evoked activity and have enhanced encoding of the meal replacement, Ensure. Finally, to directly assess the behavioral role of GC GRP+ neurons, we selectively ablated them using virally introduced caspase and monitored home-cage feeding. We found that ablation of these neurons alters meal structure by increasing its size, confirming the behavioral role of this population of neurons. Together, these studies uncover a novel neuropeptidergic mechanism within GC and may reveal new insights into how sensory cortices guide feeding behaviors.

10:15 - 12:15 PM	Bird Key
Oral Abstracts - Taste	

Chair(s): Chad Samuelsen

10:15 **The Neural Circuitry And Coding Of Interoception**

Catherine Gallori[1,2], Tianxiao Huang[1], Shiqi Wang[1], Yandan Wang[2], Verina Leung[1], Tianbo Qi[1], Alex Hiroto[1], Bohan Lin[1], Li Ye[1], Stephen Liberles[2], Chen Ran[1]

[1]The Scripps Research Institute, San Diego, CA, United States, [2]Harvard Medical School, Boston, MA, United States

The nucleus of the solitary tract (NTS) in the brainstem serves as the brain's primary interoceptive hub. It integrates and processes convergent sensory inputs from visceral organs via the vagus nerve and spinal cord, transmitting signals to higher-order brain regions to regulate behavior, physiology, and metabolism. Despite its importance, the principles by which the NTS organizes peripheral information to mediate these complex responses remain poorly understood. Here we develop a novel in vivo two-photon brainstem imaging platform, which allows us to record the activities of thousands of NTS neurons simultaneously. We discover that the NTS creates a map of internal organs that takes the shape of a "visceral homunculus". This topography requires brainstem inhibition, as blockade of inhibition broadens neuronal tuning and disrupts spatial organization. Combining brainstem imaging with genetic strategies to label targeted populations of NTS neurons, we show that the NTS creates parallel viscerosensory pathways. These pathways are distributed across the topographic map of internal organs and are similarly tuned to respond to various viscerosensory stimuli but differentially control behavior and metabolism. Our work establishes the conceptual framework of the organizational logic of the brainstem interoceptive circuits.

10:30 **Single-Cell Transcriptomics Of Tongue-Innervating Trigeminal Neurons Reveals Distinct Populations Of Pruriceptors And Mechanonociceptors**

Afshin Faridiesfanjani[1], Katherine Chacon[1], Mark Gradwell[2], Michael Kissner[3], Joriene De Nooij[4], Yalda Moayedi[1]

[1]Pain Research Center, Department of Molecular Pathobiology, New York University-College of Dentistry, New York, NY, New York, NY, United States, [2]Cell Biology and Neuroscience Department, Rutgers University, The State University of New Jersey, New Brunswick, NJ, USA W.M. Keck Center for Collaborative Neuroscience, Rutgers University, The State University of New Jersey, New Brunswick, NJ, USA., New Jersey, NJ, United States, [3]Columbia Stem Cell initiative, Columbia University Irving Medical Center., New York, NY, United States, [4]Department of Neurology Columbia University Medical Center, BB305 650 west 168th Street New York, NY 10032, New York, NY, United States

Tongue somatosensation supports several oral functions including eating, speaking and social bonding; however, the molecular identities of the peripheral sensory afferents mediating these processes remain incompletely understood. Deeper insight into lingual innervation will improve our ability to treat tongue pathologies and sensory disorders. Here, we molecularly define tongue-innervating trigeminal neurons using RNA-seq, genetic labeling, and functional imaging. Tongues of C57BL/6J mice were injected with a fluorescent retrograde tracer, and labelled trigeminal neurons were sorted for PLATE-Seq. Data were analyzed in Seurat through four steps: preprocessing, CCA-based integration with published trigeminal atlases, clustering, and visualization. Cluster markers were histologically validated. These analyses revealed eleven clusters of tongue-innervating trigeminal neurons, including peptidergic and non-peptidergic nociceptors, thermoreceptors, and mechanoreceptors. Several peptidergic populations also showed *Piezo2* co-expression, consistent with a high-threshold mechanoreceptor (HTMR) identity. Among these, two clusters co-expressed *Nefh*, indicative of an Ad identity. Notably, a single low threshold mechanoreceptor (LTMR) population was identified. *MRGPRD*-expressing pruriceptors were abundant, while *MRGPRA3*+ pruriceptors were completely absent. Consistent with this molecular profile, *in vivo* trigeminal calcium imaging revealed that tongue-innervating trigeminal neurons responded to b-alanine but not chloroquine. Overall, these findings clarify the molecular basis of tongue somatosensation, suggesting presence of not only myelinated rapidly adapting LTMRs, but also myelinated and unmyelinated HTMRs, and provide a compelling reason why lingual itch differs in prevalence from itch in other tissues.

10:45 **Microstructural Analysis Of Sucrose Licking Behavior In Rats Chronically Treated With The Glucagon-Like Peptide-1 Receptor Agonist Semaglutide.**

A. Valentina Nisi[1], Ginger D. Blonde[1], Carolina R. Cawthon[2], Emily Gallagher[1], Galina Knysh[1], Joshua Hackett[1], Jacob Scarbrough[1], Alan C. Spector[1]

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Counter to the hypothesis that the GLP-1R agonist semaglutide (SEMA) decreases the reward value and increases the satiating potency of palatable food, rats undergoing chronic SEMA treatment using a protocol emulating clinical practice with a 10-day dose escalation (ESC; 7–70 μg/kg) followed by a prolonged high-dose maintenance (MAIN; 70 μg/kg) overconsumed low to mid-range concentrations of sucrose (SUC) solution in daily 23-h two-bottle tests relative to vehicle-treated controls (VEH). Here, we tracked the drinking behavior of

non-deprived male rats presented with 1 bottle of 4% SUC in 60-min tests for 7 days before (last 2 days served as baseline; PRE) SEMA (n=10) or VEH (n=10) treatment (injected 1 h before session), during the 10-day ESC and 10-day MAIN protocol, and for 10 days after drug treatment ceased (POST). ESC, MAIN and POST data were transformed relative to PRE ($\log_{10}$(ratio)). Relative to VEH, SEMA rats reduced daily chow and total caloric intake and lost body weight (BW), despite increasing their SUC intake. These effects began to wane during POST, as the measures for SEMA and VEH rats began to converge. The number of licking bursts was higher in the SEMA rats compared to the VEH group, and this difference was also reflected in a longer meal (before 5-min pause) duration. There was no group difference in burst size. The effect of SEMA on SUC intake and several microstructural parameters became most evident during MAIN. The SEMA-induced increase in SUC intake was primarily attributable to elevated licking during the first third of the meal. Collectively, these results strongly suggest that SEMA does not decrease the reward value and appears to decrease, not increase, the satiating potency of low concentrations of sucrose solutions, at least under our test conditions.

11:00 **Juvenile Exposure To A Bitter Diet Increases Acceptance Of Quinine In Adulthood**

Verenice Ascencio Gutierrez[1], Jyothi Vasavan[1], Kamila D Nixon[1], Ann-Marie Torregrossa[1,2]
[1]Department of Psychology, University at Buffalo, Buffalo, NY, United States, [2]Center for Ingestive Behavior Research, University at Buffalo, Buffalo, NY, United States

Repeated exposure (RE) to a bitter diet increases expression of a subset of salivary proteins (SPs) which decrease bitter taste sensitivity and increase bitter acceptance. The work however has focused on adult rats on short timescales. Rodent models could offer the opportunity to look at the stability of these changes across the lifetime. It is widely known that RE during childhood can increase acceptance of bitter vegetables in children but whether the increased acceptance after RE during childhood persists into adulthood is unknown. Here, we ask if juvenile exposure increases bitter acceptance into adulthood using rodent models. Pups were weaned at postnatal day (PD) 21 onto a 0.375% quinine diet or a control diet. After 14 days all rats were given the control diet for the remainder of the study. At adult-onset (PD 65), half of the rats were tested in brief-access taste tests while the other half were given long term (22-h) acceptance tests. Brief-access animals were offered sucrose and quinine in separate tests. There was no effect of early life dietary exposure on licking to either stimulus (p's > 0.05). Long term test rats were given 22-hr access to a bottle of 1mM quinine solution. Intake was measured at 6-hr and 22-hr timepoints. Quinine-exposed rats (n=16) show greater quinine intake at 6hr ($p = 0.06$) and 22hr ($p = 0.02$) compared to control (n=17). Quinine-exposed rats also show increased burst number and burst size to quinine at the 22-hr timepoint (p's <0.05). These data suggest that early-life exposure to bitters can increase acceptance of bitter into adulthood. We are now analyzing the salivary protein signatures of both groups.

11:15 **Tissue Resident Cd8$^+$ T Cell-Mediated Inflammation Drives Bitter Sensitivity**

Pavel Nesmiyanov, Flavia Saavedra, J. Michael Stolley
Cleveland Clinic Research, Department of Inflammation & Immunity, Cleveland, OH, United States

Tissue-resident memory CD8$^+$ T cells (CD8$^+$ T_{RM}) provide durable frontline protection at barrier mucosal sites commonly exploited by pathogens as portals of entry. While extensively studied in several mucosal tissues including the gut, lungs, and urogenital mucosa, comparatively little is known about CD8$^+$ T_{RM} biology in the oral mucosa. To address this knowledge gap, we developed a model for establishing abundant antigen-specific CD8$^+$ T_{RM} in the oral mucosa of mice (oral CD8$^+$ T_{RM}). Histological studies identified that oral CD8$^+$ T_{RM} were disproportionately associated with taste papillae and isolated taste buds of the soft palate, where their local reactivation via swabbing with viral peptides triggered robust immune cell accumulation and mobilization into taste buds. Based on these observations, we hypothesized that oral CD8$^+$ T_{RM} recall responses may impact taste perception. To begin addressing this, bulk RNAseq was first performed on taste tissues isolated from mice receiving oral CD8$^+$ T_{RM} reactivation 12H earlier, where transcriptional upregulation of multiple *Tas2r* (bitter) genes were noted. Based on these findings, brief access taste testing was subsequently performed using the bitter tastant quinine, where we found that oral CD8$^+$ T_{RM} reactivation increased aversive behavior at low and intermediate concentrations. Prophylactic depletion of oral CD8$^+$ T_{RM} prior to testing abolished this response. Collectively, we provide evidence that oral CD8$^+$ T_{RM} reactivation amplifies bitter sensitivity. Future work will assess whether this phenomenon extends to other taste modalities.

11:30 **Phasic Locus Coeruleus Activation Transforms Cortical Taste Representations Across Distinct Stimulus Dimensions**

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

Norepinephrine neurons in the locus coeruleus (LC) modulate sensory responses across the brain, yet how their diverse cellular effects regulate ensemble encoding of specific sensory attributes remains unclear. To address this, we examined the influences of LC activation on the primary gustatory cortex (GC), a system rarely studied in neuromodulation. Using miniscope calcium imaging, we recorded GC excitatory neurons in mice during intraoral tastant delivery, with brief optogenetic LC activation preceding half the trials. We tested three sets of taste stimuli, each varying in a specific sensory attribute: palatability (sweet > salty > sour > bitter), mixture composition (four sucrose–NaCl ratios), and intensity (four sucrose concentrations). Across conditions, LC activation either enhanced or suppressed the responses of a subset of GC neurons, with no neuron showing both effects across stimuli. Principal component analysis revealed that LC activation increased the separation of

population responses along dimensions relevant to palatability and mixture composition. Further, LC activation rotated the coding axis for mixture composition, but not for palatability or intensity, suggesting greater invariance of the latter attributes. Scaling and rotation of coding axes were driven primarily by LC-enhanced neurons, although LC-suppressed neurons may also contribute. LC's distinct effects across conditions are partially attributable to the prevalence of additive, multiplicative, and stimulus-specific modulations at the single-neuron level. Together, our findings highlight the complexity of neuromodulatory influences on cortical coding and motivate future investigations into their underlying mechanisms and behavioral consequences.

11:45 **Don Tucker Finalist: Peripheral Taste Function Is Subject To Complex Modulation By Neuropeptide Y Family Peptides**

Satya Iyer, Ritika Gangakhedkar, Irene Bhuiyan, Jean-Pierre R. Montmayeur, Cedrick D. Dotson
Neuroscience Institute, Georgia State University, Atlanta, GA, United States

Neuropeptide Y (NPY) family peptides are known to extensively impact upon feeding behavior. Studies have also indicated that genetic knockout of NPY family peptides and receptors can affect taste responsiveness in mice, though it is unclear whether these impacts are directly mediated by peripheral taste function at the level of the tongue and the taste bud cell (TBC). Here, we found not only a direct impact of NPY family peptides on peripheral taste function but also that these impacts are dependent on the peptide and taste quality in question. Selective oral expression of peptide YY (PYY), via both viral vector and acute presentation with taste stimuli, differentially impacted bitter and fatty acid (FA)-evoked responses (i.e., suppressing bitter responsiveness and enhancing FA responsiveness). The same modulatory trends were observed when assessing stimulus-evoked calcium responses of isolated mouse fungiform TBCs *in vitro*. To validate and expand upon the translational implications of these findings we conducted *in vitro* experiments with a human fungiform TBC line and assessed functional responses to bitter and FA stimuli in the presence and absence of both PYY and NPY. While PYY modulated bitter and FA-evoked responses similarly to that observed in mice, NPY divergently impacted bitter-evoked responses while convergently impacting FA-evoked responses. NPY receptor antagonist experiments suggest that the impacts of these peptides, regardless of their similarity, were mediated by different NPY receptors. Ongoing behavioral experiments are exploring the impacts of acute NPY exposure on taste responsiveness in mice. These data strongly suggest that NPY family peptides can dynamically modulate the primary sensory input of the gustatory system to shape taste responsiveness.

12:00 **Effects Of Thermal Conditioning On Thermal-Taste Preferences In Mice**

Kyle T. Zumpano, Christian H. Lemon
University of Oklahoma, Norman, OK, United States

In ongoing work, we have found that mice can learn to prefer licking fluids at select temperatures following appetitive conditioning. It is unknown if this conditioning can interact with and affect taste preferences. Here, we studied the influence of appetitive thermal conditioning on bitter taste avoidance and the impact of TRPM8 ion channels in learning. To condition a preference for 30°C, C57BL/6J (n = 9; B6) and TRPM8 gene deficient (n = 9; M8-/-) mice were proffered 30°C 16% glucose solutions and 15°C water on alternating days over 8 days in a custom thermo-lickometer capable of controlling fluid temperature during brief access trials. A second control group (n = 9; B6, n = 9; M8-/-) was used that received water instead of glucose at 30°C. Then, both groups were proffered 15° and 30°C 0.3 mM quinine solutions in brief access tests. For M8-/- mice, a two-way ANOVA showed there was a statistically significant interaction between treatment group and temperature ($F(1,16) = 6.87$, $p = 0.019$). M8 -/- mice in the control group avoided 30°C quinine and increased licking to 15°C while mice in the treatment group were indifferent to 15° and 30°C quinine. This suggests that appetitive conditioning of 30°C decreased aversion to quinine in M8-/- mice. For B6 mice, a two-way ANOVA showed there was no significant interaction between treatment group and temperature ($F(1,16) = 0.93$, $p > 0.5$). Both the control and treatment groups licked more quinine at 15° than 30°C. This analysis is preliminary as additional cohorts will be added. These data suggest that appetitive conditioning of a temperature is sufficient to increase preference for an aversive taste stimulus when presented at that temperature in M8-/- mice.

Chair(s): Adam Dewan

10:15 **Avian Odorant Receptors: Functional Profiling And Evidence Of Gene Conversion-Mediated Evolution**

Wanting Sun, Robert Driver, Hiroaki Matsunami
Department of Molecular Genetics and Microbiology, Duke University, Durham, NC, United States

Evolution can be viewed as a dynamitic interplay between forces driving diversification and those fostering unity among species. Gene conversion, the unidirectional transfer of genetic material among homologs, can act to homogenize gene sequences in species-specific ways. While biological relevance is well documented in meiosis and human genetic diseases, its impact on the nervous system, particularly olfaction remains poorly defined. In our lab, we seek to explore this through avian odorant receptors (ORs), where a striking majority of ORs (e.g. 419 out of 473 ORs in chicken) displays extensive gene conversion mediated evolution. This unique genomic landscape allows us to address a fundamental question: *How does gene conversion balance molecular stability and adaptive flexibility in sensory evolution?* I hypothesize that alterations in the receptor's odorant ligand binding sites that avoid extensive gene conversion-mediated homogenization promotes functional diversification. Using chicken (*Gallus gallus*) as a model, my preliminary data suggest distinct odorant response profiles of ORs with high sequence similarity, and vice versa. This finding demonstrates highly structurally similar ORs (>83% similarity) can detect unique odorants, providing support for my hypothesis that through gene conversion ORs evolve to promote functional diversification. Future ongoing work will try to map the functional landscape of chicken ORs and reveal how evolutionary processes shape sensory diversity and environmental responsiveness. Ultimately, this project will establish avian ORs as a model for probing gene conversion in neural systems and recast gene conversion not only as a mechanism of genomic maintenance but also as a driver of functional innovation in the olfactory repertoire.

10:30 **Integration Of Glomerular Activity Assembles The Components Of Odor Scenes**

Kristyn Lizbinski, Gizem Sancer, Kay Ellison, Helen Mao, Madeline Albanese, James Jeanne
Yale University, New Haven, CT, United States

Natural odor scenes activate many odorant receptor types and, accordingly, many glomeruli in the brain. Projections from glomeruli activated by different components of an odor scene tend to converge onto the same higher-order neurons. For example, the scene of fermenting fruit contains volatile acids and esters which activate different glomeruli in *Drosophila,* and the corresponding projection neurons (PNs) target many of the same third-order lateral horn neurons (LHNs). However, we do not understand how, or even if, this architecture produces representations of behaviorally salient odor scenes. Here, we combine behavior, *in vivo* calcium imaging, electrophysiology, and connectome analysis in *Drosophila* to determine how LHNs process their PN inputs. We measure the responses of nearly all 51 olfactory glomeruli and 20 distinct LHN types to apple cider vinegar and 11 food-related monomolecular odorants. While apple cider vinegar is the most behaviorally attractive odor, it does not evoke the strongest response in any PN. However, it does drive the strongest response in two LHN types. Relative odor responses in these LHNs are preserved under pharmacological blockade of local inhibition, pointing to feedforward mechanisms of enhancement. Causal manipulation of PN activity during LHN recording reveals that glomeruli encoding acids and glomeruli encoding esters integrate linearly to assemble the odor scene of vinegar. A linear model also predicts much of the odor tuning across all sampled LHNs, identifying a uniform computation throughout the lateral horn. Our findings imply that LHNs encode evidence for odor scenes in a graded fashion, responding modestly to individual components and strongly to all components. The lack of nonlinearity preserves information, which likely benefits behavioral decisions.

10:45 **Sniffing As A Key Modulator Of Thalamic Salience Processing In Mice**

Janardhan P Bhattarai[1], Carolyn Mann[1], Geronimo Velazquez-Hernandez[1], Yingqi Wang[1], Brittany C Chapman[1], Sravana Nuti[1], Edgar Arturo Diaz Hernandez[1], Juee Naik[1], Tammi Coleman[1], Abby Lieberman[1], Marc V Fuccillo[1], Daniel W Wesson[2], Steven A Thomas[3], Wenqin Luo[1], Timothy A Machado[1], Minghong Ma[1]
[1]Department of Neuroscience, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, United States, [2]Department of Pharmacology and Therapeutics, Center for Smell and Taste, Center for Addiction Research and Education University of Florida College of Medicine, Gainesville, FL, United States, [3]Department of Pharmacology, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, United States

The ability to recognize and respond to important sensory stimuli is vital for survival. The paraventricular nucleus of the thalamus (PVT) plays a critical role in processing such salient information and has recently been considered as a part of the salience network. Without direct connections with sensory systems, how the PVT responds to diverse sensory stimuli remains enigmatic. To explore this, using a novel mouse line which allows genetic access to a large portion of PVT neurons, we monitored Ca^{2+} signals in the PVT via fiber photometry, simultaneously with nasal breathing recordings, in freely behaving mice. We presented a range of salient stimuli across various sensory modalities (olfactory, visual, auditory and/or somatosensory) and valences (positive or negative, innate or learned), which typically resulted in elevated PVT activity that coincided with sniffing bouts. The PVT activity is linearly scaled with stimulus-induced breathing frequency change regardless of sensory modality or valence and this relationship extends to spontaneous sniffing bouts. Artificial neural network decoding models reveal that breathing signal, but not locomotor speed, accurately predicts PVT activity. Furthermore, this sniffing-related PVT activity does not depend on respiration-entrained sensory inputs or

noradrenergic signaling mediated arousal but may result from direct input from the brainstem breathing center. Taken together, our findings suggest that the PVT responds to salient stimuli by tracking breathing frequency changes (e.g., sniffing), highlighting that sniffing-related neural signals are an integral part of salience processing within the brain.

11:00 **Alzheimer&Rsquo;S Pathobiology Detection Prior To Symptom Onset Via Olfactory Biopsy Analysis**

Vincent M D'Anniballe[1], Bradley J Goldstein[2]

[1]Duke Medical Scientist Training Program, Duke University School of Medicine, Durham, NC, United States, [2]Department of Head and Neck Surgery & Communication Sciences, Duke University School of Medicine, Durham, NC, United States

Early detection of Alzheimer's disease (AD) before cognitive decline remains a critical unmet need. Current diagnostics rely on amyloid-β and p-tau measurements in plasma or cerebrospinal fluid, rather than direct interrogation of living neuronal tissue. This limitation may obscure early pathogenic mechanisms, constrain functional assays, and contribute to ongoing debate regarding the biological relevance of observed pathology. Similar to cortical neurons at advanced disease stages, olfactory sensory neurons (OSNs) in the nasal olfactory epithelium (OE) accumulate hallmark AD pathology. However, whether detectable pathobiology impacts the peripheral OE at an early, pre-clinical stage has remained unclear. We performed endoscopically guided OE brush biopsies in adults classified by 2024 Alzheimer's Association biomarker criteria as controls (n=6), asymptomatic pre-clinical AD (n=9), or clinical AD (n=6). Single-cell RNA sequencing profiled live OE cells using experimentally validated gene expression programs, flow cytometry provided orthogonal validation. Strikingly, pre-clinical OSNs exhibited inflammatory programs previously described in postmortem AD cortical neurons. OE myeloid cells adopted an inflammatory, microglia-like state that intensified with disease progression. Concurrently, OE $CD8^+$ memory T cells exhibited elevated antigen-specific activation scores in pre-clinical AD compared with controls, mirroring cerebrospinal fluid T cell activation in clinical AD, and confirmed by increased $CD38^+HLA\text{-}DR^+CD8^+$ T cells by flow cytometry. Together, these findings support OE brush biopsies as a minimally invasive approach to capture neuronal and immune signatures of AD prior to cognitive impairment, supporting use for early detection and mechanistic discovery.

11:15 **A Double-Blind Study Of Olfactory/Sniff Training With A Randomized Blank Control Group**

Richard Doty[1], Crystal Wylie[1,3], Ronald Devere[2], Vince Groso[3], Shima Moein[3], Marco Fornazieri[4]

[1]University of Pennsylvania, Philadelphia, PA, NJ, United States, [2]Taste and Smell Disorders Clinic, Austin, TX, United States, [3]Sensonics International, Haddon Heights, NJ, United States, [4]Universidade Estadual de Londrina , Londrina , Brazil

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

11:30 **Slow-Acting Peripheral Inhibition Underlies The Behavioral Dominance Of Aversive Acidic Odors**

Kay J. Ellison, Isaiah K. Asbed, James M. Jeanne
Yale University, New Haven, CT, United States

Animals often encounter environments containing multiple odors, yet how the nervous system prioritizes them to guide behavior remains poorly understood. Here, we identify a novel form of sensory dominance in *Drosophila melanogaster* in which aversive acidic odors hierarchically control behavioral choice. When forced to choose between equally aversive acidic and non-acidic odors, flies prefer to avoid the acidic odor. Notably, acidic odors override aversion to both innately aversive odors as well as odors rendered aversive through recent learning. This dominance emerges over tens of seconds and occurs only at acidic odor concentrations that are themselves innately aversive. Using *in vivo* calcium imaging, we show that acetic acid suppresses activity in olfactory receptor neurons (ORNs) expressing Orco, which encode non-acidic odors. This suppression occurs on the same slow timescale and with the same concentration-dependence as the behavioral dominance. Interestingly, suppression occurs in both the antenna and the antennal lobe, indicating that acid dominance is implemented within the sensory periphery. In contrast, non-acidic odors have no impact on activity in ORNs expressing Ir8a, which encode acidic odors. Suppression of Orco+ ORNs is propagated to downstream projection neurons, with inhibition in both populations closely matching the temporal dynamics of behavioral dominance. Together, these results reveal that hidden odor hierarchies can emerge during decision-making and can be implemented through asymmetric inhibition between peripheral sensory channels. This represents a previously unrecognized organizing principle in olfaction. Ecologically salient chemical cues can thus shape sensory priority at the earliest stages of the nervous system, prior to higher-order integration.

11:45 **Position-Specific Olfactory Signature Among Former Professional American-Stylefootball Players**

Benoit Jobin[1,2], Colin Magdamo[1,2], Rachel Grashow[3,4], Michael Leung[3,4], Ona Wu[1,2,5], Jacob Dodelson[1,2,5], Grant Iverson[1,2,6], Marc Weisskopf[3,4], Ross Zafonte[1,2,6], Aaron Baggish[1], Mark Albers[1,2]

[1]Department of Neurology, Massachusetts General Hospital, Boston, MA, United States, [2]Harvard Medical School, Boston, MA, United States, [3]Department of Environmental Health, Harvard T. H. Chan School of Public Health, Boston, MA, United States, [4]The Football Players Health Study at Harvard University, Harvard Medical School, Boston, MA, United States, [5]Athinoula A Martinos Center for Biomedical Imaging, Charlestown, MA, United States, [6]Spaulding Rehabilitation Hospital, Charlestown, MA, United States

Olfactory deficits are well documented after traumatic brain injury, yet the integrity of the central olfactory system has not been characterized in former professional athletes exposed to repetitive head impacts. This study examined which aspects of American-style football (ASF) exposure relate to olfactory function and central olfactory system morphometry. We analyzed data from 91 former professional ASF players participating in the Football Players Health Study at Harvard University. All individuals completed a comprehensive olfactory assessment including odor discrimination (OD10), identification (OPID18), and recognition memory, and underwent structural MRI. T1-weighted MRI scans were processed with FreeSurfer to quantify volumes and cortical thickness within olfactory regions. ASF exposure variables included retrospectively reported concussion signs and symptoms, primary playing position, and years of professional and non-professional play. Participants (mean age = 49.43 ± 7.86 years; 54% Black) who played lineman positions exhibited significantly lower OD10 scores than non-linemen ($p = .049$) and odor identification scores ($p = .02$), after adjusting for age and race. Lineman status moderated the relationship between thalamic volume and odor discrimination: larger thalamic volume was associated with better discrimination among non-linemen ($p = .005$), but not in linemen ($p = .80$). Mediation analyses showed that thalamic volume did not account for the link between lineman status and OD10 score. The lineman position was negatively associated with odor discrimination, identification, and altered thalamic–function relationships. Position related exposures may differentially affect central olfactory pathways, although other mechanisms likely contribute to the observed deficits.

12:00 **A Low-Dimensional Code For Perceptual Similarity In Olfaction**

Walter Bast[1], Cina Aghamohammadi[2], Priyanka Gupta[1], Tatiana Engel[2], Florin Albeanu[1]

[1]Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, United States, [2]Princeton Neuroscience Institute, Princeton, NJ, United States

Despite recent advances, the relationship between odorant receptor (OR) activity patterns and olfactory percepts remains unclear. To investigate how OR response spectra relate to perceived stimulus similarity, we developed a novel approach that exploits the anatomical convergence of ORs onto distinct glomeruli to control sensory input at the level of individual OR types. Using two-photon and widefield imaging, we identified numerous glomeruli and determined their responses to 121 odorants. We then created synthetic olfactory stimuli by optogenetically activating selected glomerular combinations. To determine perceptual distances between these glomerular sets, we trained mice to report perceived differences between test stimuli and a reference glomerular pattern. We find that individual glomeruli within the reference set differ in perceptual relevance, as activation of some glomeruli elicits larger perceptual changes than others. To investigate whether the perceptual similarity among patterns is primarily determined by their glomerular odorant response profiles, we developed an autoencoder-based method to extract latent factors from odorant responses. This approach captured the responses of ~40 glomeruli per animal with ~90% accuracy using only ~12 dimensions. A behavioral model trained on these latent factors successfully predicted individual animals' responses to novel optogenetic stimuli. We are currently using this model to search for glomerular patterns with varying degrees of perceptual similarity to the reference percept, while confirming these predictions experimentally. Our results contribute to understanding how OR activations translate into olfactory percepts, and suggest that olfactory perception is low-dimensional and inherently structured for efficient odor representation.

12:15 - 1:30 PM	Lunch On Own
Lunch On Own	

1:00 - 2:00 PM	Bird Key
Journal Club: “How Ideas Travel: From Classic Gustatory Cortex Mapping to Modern Flavor Computations.”	

1:00 **Welcome**
Chris Lemon
University of Oklahoma

1:00 **Introduction & Historical Context - How Ideas Arise**
Joost Maier
Wake Forest University School of Medicine

1:15 **Classic Papers: 1986 Kosar Et Al., Brain Res. - Gustatory Cortex In The Rat. I. Physiological Properties And Cytoarchitecture. & 2004 Verhagen Et Al., J Neurophysiol. - Primate Insular/Opercular Taste Cortex: Neuronal Representations Of The Viscosity, Fat Texture, Grittiness, Temperature, And Taste Of Foods.**
Caitlin White
University of Louisville

1:30 **Current Paper: 2025 Allar Et Al., Current Biology - Gustatory Cortex Neurons Perform Reliability-Dependent Integration Of Multisensory Flavor Inputs.**
Donald Katz
Brandeis University

1:45 **Discussion**

1:30 - 3:30 PM	Sawyer Key
Smell Safari: Field-Based Tools for Mapping and Communicating Human Smellscapes	

To link odor exposure to human well-being (Bratman et al. 2024), track landscape-scale change (e.g., pollution effects; Quercia et al. 2015), and anchor chemosensory neuroscience in real-world odor statistics (Wachowiak et al. 2025), researchers must move beyond the laboratory and conduct controlled field studies. The proposed workshop will introduce and evaluate new methodologies for capturing, quantifying, and communicating the olfactory dimension of outdoor environments, an emerging frontier for chemosensory science. Three complementary talks will move from personal odor logging, to art-based engagement, to quantitative odor measurement, and finally to an on-site "Smell Safari" around the new AChemS venue in St. Pete, Florida. Collectively, the workshop will (i) highlight mobile and crowd-sourced approaches that scale olfactory research beyond the laboratory, (ii) demonstrate how trans-disciplinary collaborations with the arts and environmental humanities can broaden public awareness of smell, and (iii) provide attendees with an overview of sensory and psychophysical methods used in the laboratory and how they can be translated to field protocols to build georeferenced "smellscape" datasets. Lastly, the workshop will end with an interactive smell walk activity to explore and tag odors in the new St. Pete conference environment using the tools and techniques discussed. By centering smell in real-world contexts, the workshop will advance discussion on how human olfaction shapes well-being while showcasing new approaches to collecting data and capturing naturalistic smellscapes. It will also be fun! As the workshop is designed to engage trainees through both junior-investigator presentations and hands-on data collection during the concluding indoor / outdoor exercise.

Chair(s): Robert Pellegrino and Emily Mayhew

1:30 **Smellit Mobile App And Odor Awareness**
Barr Herrnstadt
Weizmann Institute of Science

1:55 **Using Art And Geography To Map Olfactory Public Spaces**
Jennifer Kitson
Rowan University

2:20 **Collecting Reliable Data To Map Odor Spaces**
Emily Mayhew
Michigan State University

2:45 **Guided Smell Safari To Quantify A New Achems Smellscape**
Emily Mayhew[1], Robert Pellegrino[2]
[1]Michigan State University, [2]Monell Chemical Senses Center

3:30 - 3:45 PM	GRAND PALM COLONNADE
Coffee Break	

3:45 - 5:45 PM	Bird Key
Clinical Symposium:Olfaction Impairment In Older Adults: Associations With Health Beyond COVID-19 and Neurodegeneration	

Sponsored in part By: Sensonics

Chair(s): Honglei Chen and Jayant Pinto

3:45 **Olfaction Impairment In Older Adults: Associations With Health Beyond Covid-19 And Neurodegeneration**

Honglei Chen
Michigan State University

Despite the recent COVID-19 pandemic, public awareness of olfactory loss in the general population remains low. This is particularly concerning for the health of older adults, as the prevalence of hyposmia increases quickly from ~6% at age 50 to ~60% by age 80. Currently, our understanding of olfactory loss and the health of older adults is limited primarily to its role as an early warning sign for neurodegenerative diseases. Emerging evidence, however, suggests that olfactory impairment may signal deteriorating health in older adults across multiple domains and may indicate accelerated aging. Furthermore, the olfactory system is uniquely positioned at the interface between the human body and the environment, offering an opportunity to explore how environmental factors may affect the health of older adults. In this symposium, we will discuss how olfaction may inform healthy aging, extending beyond COVID-19 and neurodegeneration. The first two speakers will discuss recent epidemiological findings on olfaction, physical function, and disease outcomes of aging beyond neurodegeneration. The third speaker will present multi-omics findings from cohort studies to inform the biological mechanisms and pathways linking olfaction to aging outcomes. The final presentation will brainstorm innovative ideas, identify knowledge gaps, discuss challenges, and develop strategies for exploring this concept. Notably, real-world epidemiological data from population-based studies have been underrepresented at the AChemS meeting. We anticipate that this symposium will generate significant interest among scientists at the 2026 AChemS meeting and encourage a lively discussion on new opportunities to investigate how the olfactory system connects to a range of human physiological functions in the context of aging.

3:55 **Olfaction Impairment In Older Adults: Associations With Health Beyond Covid-19 And Neurodegeneration**

Honglei Chen[1], Nicholas R Rowan[2], Yaquan Yu[1], Teresa Tian[3], Jayant Pinto[4]
[1]Michigan State University, East Lansing, MI, United States, [2]Johns Hopkins University School of Medicine Department of Otolaryngology-Head and Neck Surgery, Baltimore, MD, United States, [3]National Institute on Aging, Bethesda, MD, United States, [4]University of Chicago, Chicago, IL, United States

Despite the recent COVID-19 pandemic, public awareness of olfactory loss in the general population remains low. This is particularly concerning for the health of older adults, as the prevalence of hyposmia increases quickly from ~6% at age 50 to ~60% by age 80. Currently, our understanding of olfactory loss and the health of older adults is limited primarily to its role as an early warning sign for neurodegenerative diseases. Emerging evidence, however, suggests that olfactory impairment may signal deteriorating health in older adults across multiple domains and may indicate accelerated aging. Furthermore, the olfactory system is uniquely positioned at the interface between the human body and the environment, offering an opportunity to explore how environmental factors may affect the health of older adults. In this symposium, we will discuss how olfaction can inform and influence healthy aging, extending beyond COVID-19 and neurodegeneration. The first two speakers will discuss recent exciting findings from large epidemiological studies on olfaction, physical function, and disease outcomes of aging beyond neurodegeneration. The third speaker will present multi-omics findings from cohort studies to inform the biological mechanisms and pathways linking olfaction to aging outcomes. The final presentation will brainstorm innovative ideas, identify knowledge gaps, discuss challenges, and develop strategies for exploring this concept. Notably, real-world epidemiological data from population-based studies have been underrepresented at the AChemS meeting. We anticipate that this symposium will generate significant interest and encourage a lively discussion on new opportunities to investigate how the olfactory system connects to a range of human physiological functions in the context of aging.

4:25 **Poor Olfaction And Risks Of Pneumonia Hospitalization And Cardiovascular Diseases In Older Adults: Evidence From Two Community-Based Cohorts**

Yaqun Yuan[1], Keran Chamberlin[1], Zhehui Luo[1], Chenxi Li[1], Jayant M. Pinto[2], Eleanor M. Simonsick[3], Anna Kucharska-Newton[4], Srishti Shrestha[5], Honglei Chen[1]
[1]Department of Epidemiology and Biostatistics, College of Human Medicine, Michigan State University, East Lansing, MI, United States, [2]Section of Otolaryngology-Head and Neck Surgery, Department of Surgery, The

University of Chicago Medicine and Biological Sciences, Chicago, IL, United States, [3]Translational Gerontology Branch, Intramural Research Program of the National Institute on Aging, National Institutes of Health, Baltimore, MD, United States, [4]Department of Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States, [5]The Memory Impairment and Neurodegenerative Dementia (MIND) Center, University of Mississippi Medical Center, Jackson, MS, United States

Poor olfaction is common in older adults and may signify broader health implications beyond neurodegenerative diseases. We examined the association between poor olfaction and risks of pneumonia and cardiovascular diseases in two biracial, community-based cohorts of older adults. In the Health, Aging and Body Composition (Health ABC) Study, 2,494 participants (mean age 75.6 years; 48.4% men; 61.7% White) completed the Brief Smell Identification Test at baseline. Olfaction was categorized as good (test score 11-12), moderate (9-10), or poor (0-8). Over a median follow-up of 12.1 years, poor olfaction was associated with higher rates of total pneumonia hospitalizations (intensity ratio 1.46, 95% CI 1.22-1.75) and first-ever pneumonia hospitalization (hazard ratio 1.37, 95% CI 1.06-1.79), after accounting for potential confounding and the competing risk of death. Results were consistent across sex and race subgroups. In the Atherosclerosis Risk in Communities Study, approximately 5,800 older adults (mean age 75.5 years; 41.0% men; 77.8% White) completed the 12-item Sniffin' Sticks odor identification test at baseline. Olfaction was categorized using the same test score cutoffs as in Health ABC. During up to 10 years of follow-up, poor olfaction was associated with higher risks of incident stroke, coronary heart disease (CHD), and heart failure (HF). The multivariable-adjusted risk ratios (95% CI) for stroke were 2.14 (1.22-3.94) at year 2, 1.98 (1.43-3.02) at year 4, 1.91 (1.43-2.77) at year 6, 1.49 (1.17-2.00) at year 8, and 1.45 (1.16-1.95) at year 10. Similar associations were observed for CHD, whereas the association with HF differed slightly. Together, these findings provide evidence that poor olfaction is associated with higher risks of pneumonia and cardiovascular diseases in older adults.

4:45 **Omics Profiles Of Olfaction In Aging And Diseases**

Qu Tian, Luigi Ferrucci
National Institute on Aging, Baltimore, MD, United States

Olfaction deteriorates during aging, and olfactory deficit is an early sign of cognitive decline and neurodegenerative diseases. However, factors contributing to the loss of olfaction and the biological underpinnings of why olfaction serves as an early indicator of aging and diseases remain unclear. Potential mechanisms, such as lipid metabolism, immune responses, and diet, may be reflected in blood biomarkers. This talk focuses on omics markers of olfaction using the Baltimore Longitudinal Study of Aging data and discusses future directions and opportunities. Plasma lipid metabolites, assayed via FIA- and LC-mass spectrometry, were analyzed as six lipid classes. Plasma proteomics were assayed via the SomaScan 7k platform. Data was collected between 2015 and March 2020, before the COVID pandemic. From multivariable linear regression after adjusting for age, sex, and race, very long-chain(C22+) and long-chain(C14-C20) sphingomyelins and glycosylceramides were positively associated with olfaction (all $p<0.05$)(n=656). Very long-chain sphingomyelins and glycosylceramides attenuated and mediated the associations between olfaction and cognitive and physical functions ($\Delta\beta$:10-26%). Of 7268 proteins examined, 21 proteins were associated with olfaction ($p<0.005$)(n=380). Top-ranked proteins were involved in the regulation of epithelial cells (CFTR, CRTP1), inflammation and immune responses (S100A11, CRTP1, Calgranulin A), endothelial cells (ROBO4), motor neurons (LMO4), mitosis (UBX2B), and mitochondrial function (PRR16). The identification of plasma omics markers may shed light on the contributing factors of olfaction loss and explain its connection to aging phenotypes and diseases. Future omics studies involving larger samples and longitudinal data are warranted to provide additional mechanistic insights.

5:15 **Olfaction And The Health Of Older Adults: Knowledge Gaps, Challenges, And Strategies**

Jayant M. Pinto[1], Honglei Chen[2], Nicholas Rowan[3], Qu Tian[4], Yaqun Yuan[2]
[1]University of Chicago , Chicago, IL, United States, [2]Michigan State University , East Lansing, MI, United States, [3]Johns Hopkins Medicine, Baltimore, MD, United States, [4]National Institute on Aging, Baltimore, MD, United States

Olfactory function is closely connected to a number of health outcomes in older adults. Indeed, decreased sense of smell has been linked to physical health (pneumonia, vascular disease, stroke, heart disease, and pneumonia. Some of these relationships could explain, in part, the strong association between olfaction and cognitive health (Alzheimer's Disease and Related Dementias [AD/ADRD]). This portion of the symposium will focus on identifying knowledge gaps in mechanisms that underlie these findings, discuss challenges in designing studies that increase our knowledge in this area, and develop strategies solving these barriers. Understanding how olfaction contributes to the quality and quantity of life among older adults will reveal insights into chemosensory physiology. We will discuss how this concept could be used to slow, mitigate, or reverse the devastating consequences of olfactory and improve the lives of millions of people worldwide.

3:45 - 5:45 PM	Sawyer Key

GENES AND SENSES: GENETIC REGULATION OF CHEMOSENSATION

Chair(s): Kevin Monahan and Hojoon Lee

3:45 **Genes And Senses: Genetic Regulation Of Chemosensation**

Kevin Monahan[1], Hojoon Lee[2]

[1]Department of Molecular Biology and Biochemistry, Rutgers University, Piscataway, NJ, United States, [2]Department of Neurobiology, Northwestern University, Evanston, IL, United States

This symposium will focus on how gene regulation in chemosensory neurons modifies and shapes the perception of chemical stimuli. We highlight work at each level of perception, moving inward from the first detection of chemical compounds to central pathways that modulate the response to chemical stimuli. At the most peripheral level, perception is dictated by the expression of chemoreceptor proteins, and Thirada Boonrawd from Hojoon Lee's lab will share new findings on the expression of Tas2r bitter receptor genes by 'bitter' sensing cells in the mouse tongues. Beyond simply detecting chemical compounds, chemosensory neurons respond to changes in the chemical environment by modifying their activity and excitability. Joshua Danoff from Kevin Monahan's lab will describe new findings about how sustained neuronal activity modifies chromatin structure and gene regulation in mouse olfactory sensory neurons. Within the central nervous system, the response to chemical stimuli is modified by the state of the organism. Eirene Markenscoff-Papadimitriou will report new findings from her lab that describe how hunger status influences sensory perception by modifying gene expression and chromatin structure in rostral NTS neurons in the mouse brainstem, which acts as the first relay station from taste neurons coming in from the tongue. Finally, Monica Dus will relate new findings that explain how diet influences sensory adaptations in *D. melanogaster* gustatory neurons

3:55 **The Many Ways To Be Bitter**

Thirada Boonrawd, Syed Adnan Uddin, Hojoon Lee
Northwestern University, Evanston, IL, United States

The sense of taste allows animals to distinguish between nutritious foods and poisonous compounds in their diet. Taste receptor cells (TRCs) within taste buds express dedicated receptors to detect the five taste qualities: sweet, umami, bitter, salty, and sour. In mice, the *Tas1r2* and *Tas1r3* dimer forms the receptor for sugars. The *Tas1r1* and *Tas1r3* dimer forms the receptor for amino acids. Meanwhile, there are 35 known bitter receptors (*Tas2rs*), which are important for detecting numerous noxious compounds in the diet. Previous studies have only used dual color in situ hybridization to investigate the expression patterns of *Tas1rs* and *Tas2rs*. Therefore, the co-expression patterns of groups of *Tas2rs* remains unknown. To address this knowledge gap, we tracked co-expression of multiple *Tas2rs* and *Tas1rs* in the TRCs of the mouse circumvallate papilla and fungiform papilla using RNAscope, a multiplexed mRNA FISH method. I will present ongoing work which suggests that most *Tas2rs* often co-express together, and are usually not co-expressed with *Tas1r2*. However, we observe that some *Tas1rs* and *Tas2rs* are more broadly expressed than previously thought.

4:25 **Activity Dependent Regulation Of Gene Expression And Chromatin Structure In Mouse Olfactory Sensory Neurons**

Joshua Danoff, Kevin Monahan
Rutgers University, Piscataway, NJ, United States

Olfactory sensory neurons (OSNs) calibrate to odor environments by dampening their response to abundant odorants and heightening their response to rare odorants. This calibration requires transcriptional changes in genes that impact neuronal excitability, ultimately tuning the activity of each OSN to its environment. Using ATAC-seq and Micro-C, we investigate how chromatin structure differs in highly active and inactive neurons. 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. We then use Micro-C to compare 3D genome structures in highly active and inactive neurons, focusing on enhancer-promoter interactions at activity dependent genes. Using these approaches, we have identified how chromatin organization is modified by neuronal activity and enables expression of activity dependent genes, an essential process for olfactory sensory neurons to calibrate excitability to their environment.

4:45 **Metabolic Modulation Of Taste Processing In The Brainstem**

Eirene Markenscoff-Papadimitriou, Deepthi Vasuki, Nilay Yapici
Cornell University, Ithaca, NY, United States

5:15 **Chemosensory Neuromodulation By Extracellular Rna Transfer**

Hayeon Sung[1], Sven Barvoetz[2], Jason Shepherd[2], Sophie Caron[2], Monica Dus[1]

[1]The University of Michigan, Ann Arbor, MI, United States, [2]University of Utah, Salt Lake City, UT, United States

While it is increasingly accepted that non-neuronal support cells actively shape sensory perception, the precise molecular languages they use to converse with neurons are still being worked out. We identify the immediate

early gene Activity-regulated cytoskeleton-associated protein 1 (Arc1) as a key player in the neuromodulation of the Drosophila gustatory system. We show that sweet taste sensitivity is influences by a capsid-mediated molecular 'handshake' between thecogen support cells and sensory endings. This communication is plastic and depends on nutrient sensing. By demonstrating that support cells use viral-like capsids to transfer Arc1 and tune neuronal excitability, our findings reveal a sophisticated, cargo-specific signaling axis that is fundamental to sensory and nutritional homeostasis.

7:30 - 9:30 PM	Bird Key
Presidential Symposium: Ultra-Processed Foods, the Senses, and Health: Exploring the Evidence	

Chair(s): Yanina Pepino

7:30 **Why Do We Eat What We Eat?: Brain And Metabolic Responses To Processed Foods**
Alexandra DiFeliceantonio
Virginia Tech, Roanoke, VA, United States

Here, I will present data from studies in the lab examining the neural and physiological responses to processed foods. First, we examined acute metabolic and physiological effects of two meals matched on nutrient composition but differing in level of processing. We observe differences in blood glucose response, respiratory quotient, and energy expenditure following consumption of these meals. This difference in metabolic response correlates with neural activity in response to food pictures as measured by functional magnetic resonance imaging (fMRI). Next, to examine the longer-term effects of ultra-processed food (UPF) intake on energy intake and brain response to palatable foods, we conducted an RCT in 18–25-year-olds. This was a fully cross over trial where participants ate a diet containing 0% kcals from UPF or 81% kcals from UPF in a random order. We assessed energy intake in an ad libitum buffet meal and in an eating in the absence of hunger paradigm. We observed higher energy intake after the UPF diet intervention compared to the no-UPF diet in both tests, but only our younger cohort. There was a negative linear relationship between energy intake and age. Brain response as measured by fMRI to a palatable UPF milkshake was also altered, again in the younger cohort, with less activity in the orbito-frontal cortex after the UPF diet compared to the no-UPF diet. Taken together these data indicate the processing, even when nutrient composition is held constant, can alter acute physiological response and consumption of these diets can lead to changes in eating behavior and brain response to food, especially in younger people.

8:00 **Misspecifying Mechanisms Misleads Policy And Practical Solutions: It&Rsquo;S Not About The Processing**
John E Hayes[1,2]
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HL Mencken infamously quipped every complex problem has a well-known solution that is “neat, plausible, and wrong”. We have known for 35+ years that excessive intake of highly energy dense (ED) foods that that are high in fat, salt, and sugar (HFSS) are deleterious to health. In 2009 and 2011, the terms “ultraprocessed” and “hyperpalatable” entered the scientific literature in rapid succession; systematic critiques of these concepts emerged almost immediately, but this framing caught on quickly, resulting in hundreds of publications over the past ~15 years. Here, I will argue such framing misspecifies the problem mechanistically, and in doing so unintentionally misdirects potential solutions in terms of food reformulation and public policy. Data showing that Eating Rate and Energy Density, rather than amount of processing per se, are prime determinants of energy intake will be presented, alongside data showing that food disliking, rather than food liking, is a key driver of food intake in humans. By refocusing on these empirically supported mechanisms – Eating Rate and Energy Density – we can develop more effective interventions that actually address the root causes of excessive energy intake while preserving the pleasure from food.

8:30 **A Critical Review Of The Epidemiological, Randomized Controlled Trial, And Mechanistic Data On The Health Effects Of Ultra-Processed Foods**
Richard Mattes
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There is widespread concern about potential adverse health effects of consuming ultra-processed foods (UPF). Indeed, many nations are incorporating guidance on the intake of such items in their national policies. However, there are multiple definitions of UPF with low concordance on how to classify foods and, as result, their association with various health outcomes. To set health policy, it is desirable to have a convergence of epidemiological evidence (to established associations and at-risk populations), randomized controlled trial (RCT) data (to establish causality) and mechanistic findings (to guide interventions). To-date, there is ample, consistent epidemiological evidence linking UPF intake with adverse health outcomes. However, effect sizes are small, trends in intake are not consistent with trends in obesity (the focus of this presentation) and some sub-populations with high UPF intake have especially good health and longevity. Thus, the epidemiological evidence is still wanting. With respect to RCTs, no educational intervention has yielded beneficial effects on body weight and clinical trials show effects on food intake are transient and effects on body weight range from increased, to no change with high UPF intake, to decreased. Thus, causality has not been established. Multiple mechanisms for UPF effects on ingestive behavior and body weight have been proposed, but none, including a purported contribution of “hyper-palatability” is empirically supported. Some suggest existing data are sufficient to implement dietary guidance to eliminate UPF from the diet, but concerns about resulting increased food-borne illness, food waste, disproportionate burden on food insecure and single-parent households, and possible decreased diet quality suggest an unfavorable risk benefit assessment.

9:00 **Dopamine Signaling In Humans: Influence Of Dietary Stimulus, Metabolic State And Adiposity**
Valerie Darcey
Section on Nutritional and Metabolic Neuroimaging Diabetes, Endocrinology and Obesity Branch, NIDDK,

NIH, Bethesda, MD, United States

Central dopamine signaling is increasingly understood as a downstream integrator of sensory and metabolic information rather than a unitary “reward” signal, providing a useful framework for examining how ultra-processed foods engage the brain. Human PET neuroimaging demonstrates that dopaminergic signaling is state- and nutrient-dependent. Under fasting conditions, obesity is associated with altered dopamine signaling, whereas in the early post-ingestive state, variability in chemical sensing across oral and gut domains—rather than adiposity *per se*—shapes dopaminergic responses, appetite, and food choice. These findings suggest that the sensory and post-ingestive features characteristic of ultra-processed foods may influence dopamine signaling in ways not captured by simple reward-deficiency models. Instead, dopamine responses during the extended post-ingestive period may be particularly informative for understanding how circulating nutrients, including lipids, drive dopamine-dependent eating behavior following consumption of highly processed foods. This work parallels robust rodent evidence that intestinal nutrient sensing drives dopamine release, while highlighting key translational challenges in humans, including the optimal timing for capturing maximal post-ingestive dopamine responses. By situating dopamine within a sensory–metabolic integration framework, this work links chemoreception, internal state, and learned food preferences to mechanisms through which some ultra-processed foods may shape motivated eating behavior.

9:30 - 12:00 AM	Sawyer Key
Dance Party	