AChemS
Association for Chemoreception Sciences

ABSTRACTS

AChemS XXXV

The Association for Chemoreception Sciences
35th Annual Meeting

April 17-20, 2013

Hyatt Regency
Huntington Beach, CA

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and its commitment to advancing an understanding of the chemical senses

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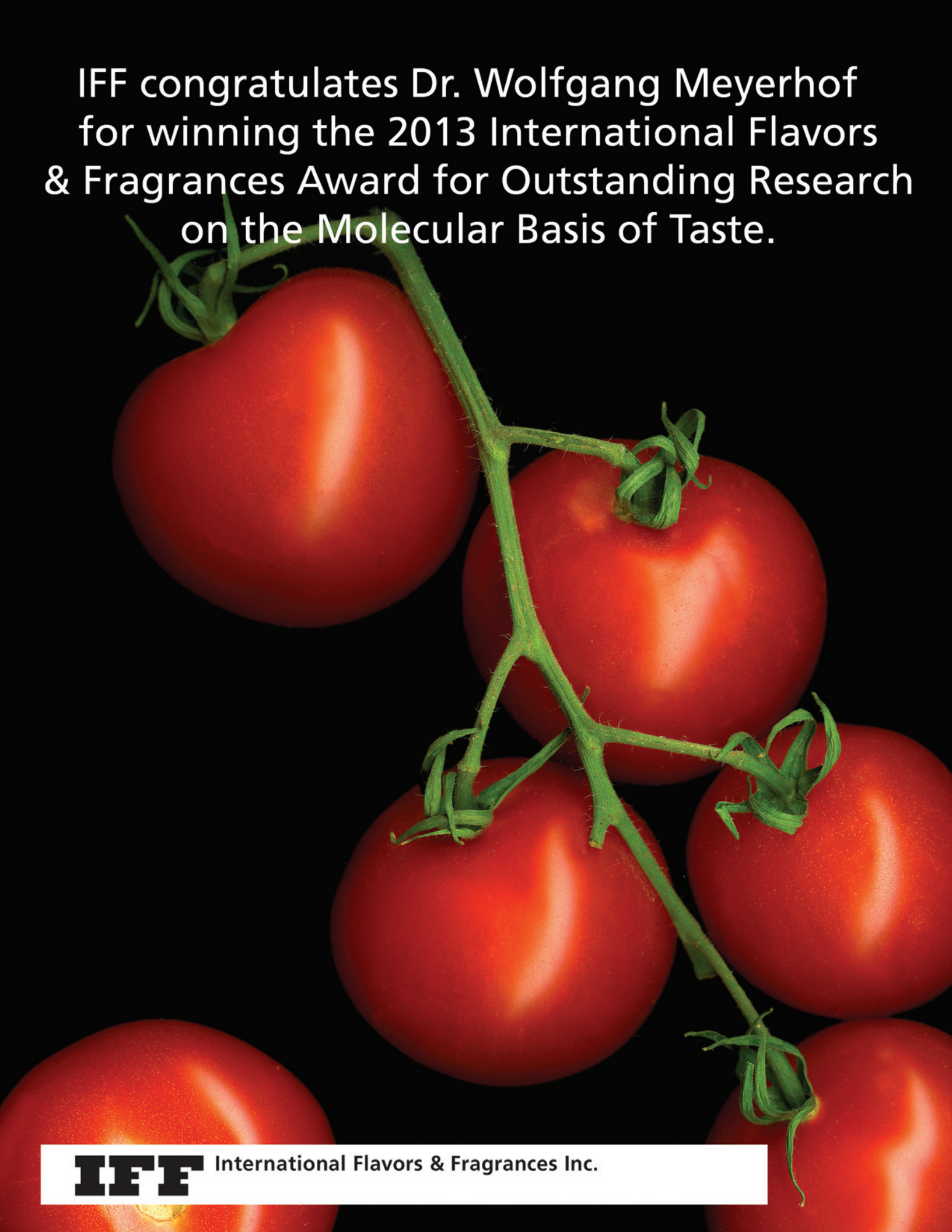

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Association for Chemoreception Sciences

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TAKASAGO

2013 Annual Meeting Exhibitors

EXHIBIT HOURS

Thursday, April 18
8:00 am – 12:00 pm

Friday, April 19
8:00 am – 12:00 pm

Saturday, April 20
8:00 am – 12:00 pm

Oxford University Press

Oxford University Press is a publisher of some of most prestigious books and journals in the world. They include Chemical Senses, the official journal of AChEMS, ECRO and JASTS. Visit our stand to pick up gratis copies of our journals, or go to **www.oxfordjournals.org** to read a free issue online.

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2013 Awardees

35th Annual Givaudan Lectureship
Bill Hansson, PhD, Max Planck Institute for Chemical Ecology, Jena, Germany

19th Annual Ajinomoto Award to Promising Young Researcher in the Field of Gustation
Peihua Jiang, PhD, Monell Chemical Senses Center, Philadelphia, PA, USA

International Flavors and Fragrances Award for Outstanding Research on the Molecular Basis of Taste
Wolfgang Meyerhof, PhD, German Institute of Human Nutrition, Nuthetal, Germany

22nd Annual Moskowitz Jacobs Award for Research in Psychophysics of Human Taste and Smell
Wen Li, PhD, University of Wisconsin-Madison, Madison, WI, USA

Max Mozell Award for Outstanding Achievement in the Chemical Senses
Stuart Firestein, PhD, Columbia University, New York, NY, USA

The AChemS Young Investigator Award for Research in Olfaction
Haiqing Zhao, PhD, Johns Hopkins University, Baltimore, MD, USA

The Don Tucker Memorial Award (2012 Awardee)
Cecil "Jake" Saunders, The University of Colorado, Aurora, CO, USA

The Polak awards are funded by 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

Polak Young Investigator Award Recipients
Pablo Chamero, University of Saarland, Homburg, Germany
Adam Dewan, Northwestern University, Evanston, IL, USA
Dany Gaillard, University of Colorado Denver, Denver, CO, USA
Ahmad Jezzini, SUNY, Stony Brook, NY, USA
Kathrin Ohla, German Institute of Human Nutrition, Nuthetal, Germany
Markus Rothermel, University of Utah School of Medicine, Salt Lake City, UT, USA

2013 Awardees

We are pleased to announce that five 2013 Polak Junior Scientist Travel Awards were given for this year's Meeting.

AChemS Travel Fellowships for Diversity Recipients:
Funded by a generous grant from the National Institute on Deafness and Other Communication Disorders and the National Institute on Aging, NIH
Norma Castro, San Diego State University, San Diego, CA, USA
Deandrea Ellis, Columbia University, New York, NY, USA
Melissa Haley, Stony Brook University, Stony Brook, NY, USA
Mavis Irwin, University of Utah, Salt Lake City, UT, USA
Yasmin Marrero, Brandeis University, Waltham, MA, USA
Jacquelyn Szajer, San Diego State University, San Diego, CA, USA
Cedric Uytingco, University of Maryland School of Medicine, Baltimore, MD, USA

AChemS Student Housing and Travel Award Recipients
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Darcy Trimpe
Cedric Uytingco
Megha Vasavada
Crystal Wall
Pei Xu
Wendy Yoder
Shaohua Zhao
Harriët Zoon

Logo Award Winner
Cedric Uytingco, University of Maryland, School of Medicine, Baltimore, MD, USA

Committees

ACHEMS EXECUTIVE COMMITTEE 2012-2013

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Bettina Malnic
John McGann
Steve Munger
Venky Murthy
Brian Smith
Mark Stopfer
Lisa Stowers
Ali Ventura
Paul Wise

MEETING EVALUATION

The meeting evaluation is available online this year. Please visit **www.achems.org** to give us your feedback on the meeting. Your input helps AChemS' leadership continue to offer quality annual meetings and member services.

Oral Abstracts

#1 GIVAUDAN LECTURE: NON-MODEL MODELS IN OLFACTION

Bill S. Hansson
Max Planck Institute for Chemical Ecology, Jena, Germany

Our knowledge regarding olfactory structure and function has taken a quantum leap since the characterization of putative olfactory receptors both in vertebrates and insects. Still, the understanding of both ecological and evolutionary processes is lagging behind. What do different odors really mean to animals, and how has the system evolved to allow them to respond behaviorally in a relevant manner. To understand these topics better we use both a model insect (*Drosophila melanogaster*), and a number of non-model arthropods (moths, ants, primitive insects, land-living crustaceans).

I will spend a short introductory part on recent progress in our work on drosophilid flies, touching on investigations of hard-wired smell-driven behavior. The rest of my talk I will devote to non-model arthropods.

In the desert ant, *Cataglyphis fortis*, we have built on the classic investigations by the group of Rüdiger Wehner in Zürich. They demonstrated the amazing ability of these tiny insects to find their way home in a salt desert using vector-based orientation. In our investigations we show how the ants use odor cues to pinpoint their nest entrance, but how this orientation is, in a life-saving fashion, weighed against vector orientation. We also show how the ants use olfactory cues to find their main source of food; dead insects, in a highly efficient way, and how this smell-based food search is independent of the home vector.

To investigate the evolution of arthropod olfactory systems we make use of both highly primitive, archeopteran insects (in comparison to their neopteran relatives), and of land-living crustaceans that have entered the terrestrial environment during the last five million years. Using a combination of transcriptomics, electrophysiology, morphology and bioassays we show that the neopteran divide coincides with a drastic development in the insect olfactory system, and that some land-living crustaceans have developed enormous central olfactory systems, while others seem to have abandoned olfaction.

#2 SYMPOSIUM: THE STRUCTURAL BASIS OF CHEMOSENSORY SIGNALING

G protein coupling GPCRs: structural and functional insights into reciprocal G protein and GPCR interactions

Roger K. Sunahara
University of Michigan Medical School Ann Arbor, MI, USA

Recent advances in the structural biology of G protein-coupled receptors have helped to unravel the intricacies of ligand binding. Similarly structural and biochemical analyses of heterotrimeric G proteins have affirmed our understanding of the mechanism underlying effector interactions and GTPase activity. The recent crystal structure of a prototypic GPCR, the beta$_2$-adrenergic receptor (beta$_2$AR), in a complex with the stimulatory G protein, Gs, trapped in its nucleotide-free state, has now provided models for activation of G proteins by GPCRs. These data have helped to delineate how hormone binding to GPCRs leads to GDP release on G proteins, the principle step that precedes GTP binding and G protein activation. The crystal structure, together with data from single particle reconstructions by electron microscopy and deuterium exchange mass spectrometry, reveal dramatic changes in the G protein alpha-subunit. The structural data also suggest that G proteins may allosterically regulate the receptor by stabilizing a closed conformation on the extracellular face of the receptor. Radioligand binding analyses suggest that G protein coupling slows ligand dissociation, consistent with the observed structural changes in the extracellular face. Such structural changes account for the slower observed ligand dissociation rates and likely account for G protein-dependent high affinity agonist binding. Together these data support a plausible model for the mechanism for receptor-mediated nucleotide exchange, G protein activation and agonist binding.
Acknowledgements: GM083118

#3 SYMPOSIUM: THE STRUCTURAL BASIS OF CHEMOSENSORY SIGNALING

Structural Determinants of TRPV Channel Activation and Desensitization

Rachelle Gaudet
Harvard University Cambridge, MA, USA

My lab is broadly interested in the mechanisms of signaling and transport across cellular membranes. Much of our research centers on TRP channels and their role in sensory perception. We focus on temperature-sensitive ion channels, particularly TRPV1 and TRPA1. TRP channels are challenging structural biology targets because they are large multidomain eukaryotic membrane proteins and are not naturally abundant. We take complementary approaches to obtain structural and functional information on TRP channels. One strategy is to divide and conquer: determine crystal structures of isolated domains of TRP channels. The results can then combined with

genetic, biochemical and physiological data to advance our understanding of TRP channel function. It also provides valuable insights as we tackle the structure determination of whole TRP channels. Acknowledgements: NIH grant R01GM081340 to RG.

#4 SYMPOSIUM: THE STRUCTURAL BASIS OF CHEMOSENSORY SIGNALING

Atomistic Structures of human olfactory and taste receptors

William A Goddard, Soo-Kyung Kim, Ravinder Abrol
Materials and Process Simulation Center, California Instute of Technology Pasadena, CA, USA

Olfactory receptors (ORs) responsible for mediating the sense of smell are G protein-coupled receptors (GPCRs). Through differential interactions the ~400 ORs allow us to recognize countless ligands. However little is known about the specific interactions responsible. We use first principles (non homology) methods to predict the ensemble of 24 low energy structures for the human OR1G1 (hOR1G1) using the GEnSeMBLE (GPCR Ensemble of Structures in Membrane BiLayer Environment) method. The final best structure has strong interhelical H-bonding networks in TMs 1-2-7 (N1.50, D2.50 and N7.49), and TMs 2-4 (N2.45 and W4.50), which have been observed in x-ray and predicted structures for some members of the class A (rhodopsin family) GPCRs. We also find a salt-bridge between the conserved D3.49 and K6.30 in the D(E)RY region, associated with the inactive form for class A GPCRs. In addition, a hOR specific interaction was formed between the conserved D/E3.39 and H6.40 in hORs, which might be an important conformational constraint in all hORs since they are highly conserved (~94 and 98% respectively) among all hORs. We expect our predicted 3D structures for hOR1G1 to provide a guide in understanding the structural patterns for all hORs. This might help design better odorants for foods and perfumes and improved drugs for neurodegenerative disorders, such as anosmia (inability to detect odors) or hyposmia (decreased ability to detect odors). The structure and conserved elements of the hORs are compared to our recent prediction of the atomistic structure for the human TAS2R38 Bitter Receptor.

#5 SYMPOSIUM: THE STRUCTURAL BASIS OF CHEMOSENSORY SIGNALING

Comprehensive mapping of functional sites for agonists and inhibitors of the bitter taste receptor TAS2R16

Joseph B. Rucker
Integral Molecular Philadelphia, PA, USA

Bitter tastes are detected at the cellular level by a diverse family of taste receptors (TAS2Rs) belonging to the G protein-coupled receptor (GPCR) superfamily. The lack of direct structural information for TAS2Rs (and most GPCRs) limits our understanding of their structural features responsible for ligand binding and signaling. Using a high-throughput approach called Shotgun Mutagenesis Mapping, we created a comprehensive TAS2R16 mutation library with defined point mutations at every amino acid in the receptor and screened each mutant's functional activity in response to unique ligands, both agonists and inhibitors, using a Ca^{2+}-flux signaling assay. We identified amino acids that, when substituted, abrogate signaling for all agonists, as well as residues important for the activity of only specific ligands. These critical residues define both the binding sites for various TAS2R16 ligands as well as motifs important for signal transduction, and will help guide the structural understanding of bitter taste receptor function. Acknowledgements: NIH DC002995 NIH DC010105 NIH GM072379

#7 INDUSTRY SYMPOSIUM: TASTE AND SMELL IN TRANSLATION: APPLICATIONS FROM BASIC RESEARCH

Individual differences in oral fat detection and their health implications

Richard Mattes
Purdue University, West Lafayette IN 47907 USA

The fat content of foods and the oral perception of this fat influence food choice and a wide range of physiological responses with health implications. Triacylglycerol, the predominant form of dietary fat, generally contributes positive somatosensory attributes to foods and are viewed as orexigenic. In contrast, non-esterified fatty acids, likely taste stimuli, typically elicit negative hedonic responses and are anorexigenic. The latter also exerts unique effects on cephalic, intestinal and post-absorptive lipid metabolism. However, individual variability in taste and physiological responses is extremely high raising question about distinct groups of fat tasters/responder This presentation will examine possible sources of individual variability such as learning, BMI status, age, gender and stimuli properties to facilitate better study designs and interpretation of the functions of "fat taste."

#8 INDUSTRY SYMPOSIUM: TASTE AND SMELL IN TRANSLATION: APPLICATIONS FROM BASIC RESEARCH

Mechanisms for Fat Taste

Timothy Gilbertson
Department of Biology, Utah State University, Logan UT 84322 USA

It has been well over a decade since our laboratory first identified the ability of free fatty acids to activate mammalian taste receptors cells, consistent with there being a "taste of fat". Since that time, the ability of fatty acids to act as the proximate stimuli for fat taste has been validated in a number of species spanning the molecular, cellular and behavioral levels. We have recently identified several novel fatty acid-activated G protein-coupled receptors that, in conjunction with the fatty acid binding protein CD36, allow the recognition of chemically distinct classes of free fatty acids. This presentation will summarize what is known about the receptors and transduction pathway for free fatty acids.

#9 INDUSTRY SYMPOSIUM: TASTE AND SMELL IN TRANSLATION: APPLICATIONS FROM BASIC RESEARCH

Insights from olfactory receptor screening

Joel Mainland
Monell Chemical Senses Center, Philadelphia PA 19104 USA

A major advances in the taste field in recent decades was the identification of receptors that mediate taste. Expression of these receptors in heterologous cell-based assays has allowed scientists in both academia and industry to screen for novel taste agonists, antagonists, and modifiers. Similar studies in olfactory receptors have lagged behind the taste field due to the size of the receptor family as well as difficulties in expressing the receptors in heterologous cells. In this talk we will explore the current state of the science in olfactory receptor screening, relationships between odorant structure and odor quality, and the identification of agonists, antagonists and modifiers for olfactory receptors.

#10 INDUSTRY SYMPOSIUM: TASTE AND SMELL IN TRANSLATION: APPLICATIONS FROM BASIC RESEARCH

Mechanisms of olfactory adaptation

Haiqing Zhao
Johns Hopkins University, Baltimore MD 21218 USA

Olfactory receptor cells exhibit reduced sensitivity upon prolonged or repeated odor exposure—a phenomenon known as adaptation. Adaptation at the cellular level is thought to underlie, at least in part, the perceptual desensitization of an odor over time. In vertebrates, several calcium-dependent feedback mechanisms have been proposed to account for adaption of olfactory receptor cells. Recent studies using molecular genetic approaches that allow selective disruption of these calcium-dependent mechanisms have provide new insight into how olfactory adaptation may occur.

#12 PRESIDENTIAL SYMPOSIUM: GUT PEPTIDE INTERACTIONS BETWEEN TASTE, FEEDING, AND REWARD

Bariatric surgery and appetite

Carel Le Roux
Experimental Pathology, UCD Conway Institute, School of Medicine and Medical Science, University College Dublin, Ireland

A good model to investigate appetite reduction in humans and rodents with associated major weight loss is bariatric surgery. Gastric bypass, but not gastric banding caused increased postprandial PYY and GLP-1 favouring enhanced satiety. An early and exaggerated insulin response mediates improved glycaemic control. The rodent model of bypass showed elevated PYY, GLP-1 and gut hypertrophy compared with sham-operated rats. Moreover, exogenous PYY reduced food intake while blockade of endogenous PYY increased food intake. A prospective follow-up human study of gastric bypass showed progressively increasing PYY, enteroglucagon, and GLP-1 responses associated with enhanced satiety. Blocking these responses in animal and human models leads to increased food intake. Thus, following gastric bypass, a pleiotrophic endocrine response may contribute to improved glycaemic control, appetite reduction, and long-term lowering of body weight. We have shown that changes occur in the sensory, reward and physiological domains of taste that may mechanistically contribute to the alterations in food preferences after gastric bypass. The sustained nature of weight loss, reduced appetite and shifts in food preferences may be explained by gut adaptation and chronic hormone elevation.

#13 PRESIDENTIAL SYMPOSIUM: GUT PEPTIDE INTERACTIONS BETWEEN TASTE, FEEDING, AND REWARD

Common Mechanisms of Alimentary Chemosensation: Implications for Taste, Ingestion and Glucose Homeostasis

Steven D. Munger[1,2]
[1]University of Maryland School of Medicine, Department of Anatomy and Neurobiology Baltimore, MD, USA, [2]University of Maryland School of Medicine, Department of Medicine Baltimore, MD, USA

The last two decades has seen a growing recognition that a common molecular toolkit is employed along the length of the alimentary canal to detect and respond to nutrients. For example, many of the same proteins that are critical for recognizing sweet, bitter and umami taste stimuli in the mouth, including T1R and T2R taste receptors and the transduction proteins α-gustducin and TRPM5, are found throughout the gastrointestinal (GI) tract and associated organs. Similarly, taste buds express a number of neuropeptides that are perhaps best understood in other systems as endocrine factors that impact nutrient metabolism and/or ingestive behaviors. A better understanding of the molecular mechanisms that couple nutrient detection to peptide secretion in gustatory and GI tissues could lead to the identification of new pharmacological targets for impacting ingestion, satiety, nutrient assimilation or glycemic control. I will discuss our recent studies in rodents, including animals deficient in specific taste receptor subunits or receiving Roux-en-Y gastric bypass, that provide new insights into the mechanisms of nutrient response in the mouth and gut and the role of these mechanisms in taste coding, post-ingestive nutrient response, and the regulation of glucose homeostasis. Acknowledgements: NIDCD (DC010110), Tate & Lyle Americas, Ajinomoto Amino Acid Research Program

#14 PRESIDENTIAL SYMPOSIUM: GUT PEPTIDE INTERACTIONS BETWEEN TASTE, FEEDING, AND REWARD

GLP-1 neurons: A link between gastrointestinal satiation signaling and food reward?

Diana L. Williams
Psychology Department & Program in Neuroscience, Florida State University Tallahassee, FL, USA

Central glucagon-like peptide 1 receptor (GLP-1R) stimulation suppresses food intake, and hindbrain GLP-1 neurons project to numerous feeding-relevant brain regions. One such region is the nucleus accumbens (NAc), which plays a role in reward and motivated behavior. Using immunohistochemical and retrograde tracing techniques in rats, we identified a robust projection from GLP-1 neurons in the nucleus of the solitary tract to the NAc core. Our pharmacologic studies then provided evidence that exogenous and endogenous GLP-1R stimulation in the NAc core reduces food intake. The NAc is known to influence food palatability and motivation, while GLP-1 neurons have been implicated in mediation of meal-related gastrointestinal signals. We hypothesize that GLP-1 released in NAc in response to nutrient ingestion contributes to meal-induced satiation, and that GLP-1 action in NAc reduces the hedonic value of food.
To understand the role of endogenously released GLP-1 in the NAc core, we have been performing detailed behavioral analysis of the effects of blockade of GLP-1R at this site. We find that injection of the GLP-1R antagonist exendin 9-39 (Ex9) into the NAc core selectively increases meal size and blunts the satiating effects of nutrients. In rats consuming sucrose solutions, NAc core Ex9 treatment increases initial lick rate and duration of licking bursts. These measures are directly correlated with palatability, so this supports the idea that endogenous GLP-1R stimulation in NAc reduces the hedonic value of food. We continue to use other behavioral approaches to discern effects on palatability and motivation for food. Together, our data support the suggestion that the GLP-1 projection to NAc serves as a link between gastrointestinal satiation signaling and hedonic aspects of eating. Acknowledgements: Supported by DK078779

#15 PLATFORM PRESENTATIONS: OLFACTION

Lateral inhibition and odor mixture integration among distinct subpopulations of olfactory bulb output neurons imaged in vivo

Michael N Economo, Matt Wachowiak
Brain Institute and Department of Physiology, University of Utah Salt Lake City, UT, USA

While lateral inhibition between functional processing units is a fundamental feature of sensory systems, the organization of lateral inhibitory circuits in the olfactory system and their impact on odor representations remain unclear. Here, we addressed this question in the olfactory bulb (OB) using in vivo two-photon imaging from genetically-defined OB output neuron populations. We optically recorded activity from mitral and deep tufted (MT) cells projecting to piriform cortex and from cholecystokinin-expressing superficial tufted (ST) cells using Cre-dependent expression of the genetically-encoded fluorescent calcium indicators GCaMP3 and GCaMP5G. We compared lateral inhibition to these different populations using pairs of monomolecular odorants that activated distinct neuron subsets and their binary odorant mixtures. Both MT and ST populations showed detectable mixture suppression in a fraction of neurons (31% for MT vs. 36% for ST cells), reflecting lateral inhibition between cell ensembles with distinct odorant response specificities. However, in these neurons the magnitude of this suppression was significantly stronger in MT cells vs. ST cells (70% vs. 25% suppression by the mixture). Thus, these different OB output populations - which project to distinct cortical targets - integrate olfactory information differently. In addition we found that odorants often evoked fluorescence decreases in MT somata and glomerular neuropil in a reliable, odorant-specific manner, likely reflecting inhibition of spontaneous activity in these neurons. These experiments thus enable us to, for the first time, directly map the spatial organization of lateral inhibition in vivo and to characterize how this inhibition varies across different cell types and OB layers as it shapes early odor representations. Acknowledgements: NIH NIDCD R01 DC006441 NIH NIDCD 1F32DC012718-01

#16 PLATFORM PRESENTATIONS: OLFACTION

AWnt5 Gradient Patterns the *Drosophila* Olfactory Map

Huey Hing[1], Yuping Wu[2], Lee Fradkin[3], Jasprina Noordermeer[3]
[1]SUNY Brockport/Biology Brockport, NY, USA, [2]Stowers Institute for Medical Research Kansas City, KS, USA, [3]Leiden University Medical Center/Molecular Cell Biology Leiden, Netherlands

Although the olfactory map facilitates the encoding of odor information, how its pattern is specified remains largely unknown. Recent work has shown that the *Drosophila* olfactory map is initially formed by spatial segregation of the projection neuron dendrites in the antennal lobe. Here we demonstrate that the Wnt5 protein specifies projection neuron dendrite positions prior to arrival of the olfactory receptor axons. Wnt5 is expressed by a novel set of guidepost cell neurons which are located at the dorsolateral pole of the antennal lobe and generate a dorsolateral to ventromedial gradient of Wnt5 in the nascent antennal lobe neuropil. Loss of *wnt5* prevents the appropriate ventral migration of the projection neuron dendrites while over-expression of *wnt5* severely disrupts dendritic patterning. We also show that Drl, a known Wnt5 receptor, acts cell-autonomously in the projection neurons to repress the Wnt5 signal. Decreased *drl* function causes projection neuron dendrites to inappropriately target ventromedially; a defect which is strongly suppressed by loss of a copy of the *wnt5* gene. We propose that the Wnt5-secreting guidepost cells act to provide positional information to the projection neuron dendrites. Our findings demonstrate the importance of a Wnt5 gradient in the patterning of the olfactory map. Acknowledgements: DC010916-01

#17 PLATFORM PRESENTATIONS: OLFACTION

Sexual dimorphism and experience-dependent plasticity in mouse vomeronasal neurons

Timothy E Holy, Pei S Xu
Washington University in St. Louis St. Louis, MO, USA

Male and female mice exhibit behaviors particular to their sex, and these differences presumably reflect sexual dimorphism in neuronal circuitry. However, in terms of neuronal anatomy or function in the mouse, there are relatively few reported differences males and females. Here we asked whether neurons in the vomeronasal organ, a social odor- and pheromone-sensing neuroepithelium, differed functionally between males and females. We performed exhaustive high-speed calcium imaging from intact vomeronasal epithelia in 26 imaging volumes from male and female mice, measuring the responses of more than a quarter-million individual sensory neurons. Using a battery of sulfated steroids, a class of odors originally isolated from mouse urine, we found that the large majority of responsive neuronal types were found in equal abundance in both males and females. However, we found restricted cases of clear sexual dimorphism, including one neuronal type that was more than one-hundred-fold more common in males than in females, by far the strongest dimorphism ever reported in the mammalian central nervous system. We then explored the mechanism generating this dimorphism. Surprisingly, male/female differences depended entirely on the history of sensory experience, as vomeronasal organs from males could be converted to a pattern indistinguishable from females simply by prolonged exposure to the odors of female mice. The finding that a strong neuronal dimorphism is determined entirely by experience, in a sensory system long believed to be devoted to "innate" responses, raises important new questions about the roles of "nature" and "nurture" in brain architecture. Acknowledgements: NIH-NIDCD R01 DC005964 NIH-NINDS/NIAAA R01 NS068409 NIH DP1 OD006437

#18 PLATFORM PRESENTATIONS: OLFACTION

Reinforcement of Sexual Attraction through Pheromone-Induced Associative Learning

Jane L Hurst, Sarah A Roberts, Emma Hoffman, Amanda J Davidson, Lynn McLean, Robert J Beynon
University of Liverpool / Institute of Integrative Biology Liverpool, United Kingdom

Scents play an integral role in mediating reproductive interactions in many species, allowing animals to recognize and locate individual conspecifics of the opposite sex, assess their attractiveness and stimulate mating. The urine used by male house mice to advertise their location and competitive dominance contains many androgen-dependent volatiles together with a high concentration of major urinary proteins (MUPs) that bind and slow the release of these volatiles. Females that detect airborne urinary volatiles are attracted to approach and sniff the scent marks closely, but it is contact with an atypical male-specific MUP named darcin that reliably elicits female sexual attraction to spend time near male scent. Darcin will elicit this attraction even in the absence of all other urinary components, while male urine without darcin is no more attractive than female urine. Importantly, though, darcin acts not only through direct attraction to spend time near the pheromone itself. It is also highly potent in stimulating associative learning such that animals rapidly learn the same attraction towards the individual airborne odor detected in association with darcin, targeting attraction to a specific male. Darcin also rapidly conditions preference for spatial cues associated with its location, such that mice relocate and prefer to spend time in the site even when scent is absent. This conditioned place preference is remembered for approximately 14 days. Preference for multiple locations can be remembered, while the relative amount of darcin in competing male scents influences female conditioned preferences. This reveals that pheromone-induced social learning can both target and strongly reinforce female sexual attraction towards individual males even though male mice all produce the same sex pheromone. Acknowledgements: These studies were supported by the Biotechnology and Biological Science Research Council (BBC503897 and BB/J002631/1) and the Natural Environment Research Council (NE/G018650), UK

#19 PLATFORM PRESENTATIONS: OLFACTION

Behavioral effects of bulbar neuromodulation

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The olfactory bulb (OB) is modulated by a number of extrinsic and intrinsic modulatory substances. We here synthesize work from our lab investigating the effects of cholinergic (ACh), noradrenergic (NE), serotonergic (5HT), dopaminergic (DA) and hormonal modulation on olfactory perception. We compare the behavioral effects by using well–established behavioral paradigms such as olfactory habituation memory and reward-association. We find that ACh modulation affects the discrimination of chemically and perceptually similar odorants (Mandairon et al. 2006; Chaudhury et al. 2009), with specific roles for muscarinic and nicotinic receptors (Devore et al., in prep). NE, while also modulating odor discrimination of chemically and perceptually similar odorants (Mandairon et al. 2006; see also Doucette et al. 2007), also plays a specific role in regulating signal to noise ratio when very low concentration odorants are used (Escanilla et al 2010). In a direct comparison, NE, but not ACh, is shown to be functionally important during learning of very low concentration odorants (Escanilla et al 2012). DA, intrinsic to the bulb, modulated odor concentration perception via activation of D2 but not D1 receptors (Escanilla et al. 2009). Blockade of 5HT receptors impaired habituation memory formation and specificity, as well as reward-driven discrimination at low, but not higher odor concentrations (Lewis and Linster, in prep). Both hormonal (estrodial, in mice) and NE manipulations (in rats) extended the duration of an olfactory habituation memory (Dillon et al, in prep; Manella et al. in prep). In summary, the behavioral effects of OB neuromodulators, while similar at first

sight, can be dissociated to ascribe specific roles to each of these substances when task demands are manipulated in different ways. Acknowledgements: NIH/NIDCD RO1DC009948 NIH/NIDCD RO1DC008701 NIH/NIDCD F32DC011974 l'Oreal USA fellowship for women in science

#20 PLATFORM PRESENTATIONS: OLFACTION

Olfactory Dysfunction Predicts 5-year Mortality in Older Adults

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We sought to determine if loss of olfactory function among older US adults is a harbinger of overall health decline predicting 5-year mortality. In 2005-6 The National Social Life, Health and Aging Project (NSHAP) interviewed 3,005 adults aged 57-85 (Wave 1) representative of the diverse aging US population. Olfactory function was measured with 5 Sniffin' Sticks pens and word/picture prompts to classify participants as normosmic (4-5 correct), hyposmic (2-3 correct), or anosmic (0-1 correct). Five years later NSHAP Wave 2 established participant mortality. Logistic regression used olfactory function at Wave 1 to estimate the odds of death at Wave 2, controlling for baseline factors known to influence both olfaction and mortality (age, gender, education, race/ethnicity, cognitive function, physical and mental health, and tobacco/alcohol use). Olfactory identification at Wave 1 strongly predicted subsequent 5-year all-cause mortality: fully 39% of anosmic subjects had died compared to 19% in the hyposmic group and 10% in the normosmic group ($p<0.001$). This "dose-dependent" effect was not explained by potential mediating factors, including number of comorbid diseases, demographics and cognitive function. In a comprehensive model, anosmic participants had three times the odds of death compared to normosmics (OR 3.00, 95%CI 1.66, 5.42, $p<0.001$). Moreover, the increased odds of death occurred in all age groups (57-64, 65-74, and 75-85 years). Our results suggest that a simple olfactory test may have clinical utility in predicting 5-year mortality. Possible physiological mechanisms linking olfactory loss and death include slowed cellular regeneration and repair or sentinel function as a marker of toxic environmental exposures or neurologic decline. Acknowledgements: The National Institute on Aging (R37 AG030481 AG036762 AG029795), the Institute for Translational Medicine at The University of Chicago (KL2RR025000), the McHugh Otolaryngology Research Fund, and the American Geriatrics Society.

#21 PLATFORM PRESENTATIONS: OLFACTION

The Scent of a Human: A Mosquito Olfactory Receptor Neuron that Mediates Attraction to Human Skin Odor

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Mosquitoes that feed on humans transmit deadly diseases that affect hundreds of millions of people every year. Host-seeking females use a combination of carbon dioxide and skin odor cues to find human hosts. Even though whole skin odor is attractive by itself, specific compounds have not been identified that are attractive in the absence of a CO_2 plume. We use electrophysiology assays to identify a specific olfactory receptor neuron (ORN) class that responds to whole skin odor. From the human odor blend, we identify specific compounds that activate this ORN strongly. This response is conserved in both *Aedes aegypti* and *Anopheles gambiae*, even though these two species, both of major public health importance, are not closely related. We specifically suppress the activity of this ORN for hours by treatment with a reactive compound that is structurally related to known ligands. After treatment, mosquitoes show deficits in navigation toward human skin odor in a wind tunnel. This is among the first ORN classes shown to play a role in attraction to skin odor. The receptors expressed in this ORN are highly conserved, offering hope that compounds that affect their activity can be used in a new generation of economical and environmentally friendly lures and repellents for mosquito control. Acknowledgements: NIH grant RO1AI087785 and R56AI099778. GMT partly supported by UC Global Health Institute and Bill and Melinda Gates Foundation.

#23 SYMPOSIUM: STEM AND PROGENITOR CELLS FOR TASTE BUDS — DEVELOPMENT AND RENEWAL

Signaling compartments regulate development and maintenance of stem, progenitor and differentiated cells in taste papillae and taste buds

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Stem and progenitor cell biology is based in spatial and temporal contexts of compartments or niches where a supporting signaling environment sustains stem and progenitor properties. Thus for taste bud stem or progenitor cells, we must examine: epithelial, mesenchymal and specialized cells in tongue, papilla and taste bud, in embryo, early postnatal and adult stages. Principles and knowledge about stem/progenitor cell biology in compartment and stage specific contexts will be presented. Current thinking is applied with the example of sonic hedgehog (Shh) signaling in regulating lingual tissue, fungiform papilla and taste bud development and maintenance, and epithelial/mesenchymal exchanges including contributions from neural crest. The data locate Shh ligand and Shh responding cells; bring new findings of Shh roles in tongue, papilla and taste bud development and

maintenance; demonstrate a contribution of Shh responding, Gli1 labeled progeny to taste bud cells and cells of the papilla; and present distinctive effects of activating Shh transcription factors in adult tongue. Defined proliferation niches of active Shh signaling suggest that epithelium and mesenchyme harbor multiple stem and progenitor cell compartments. In sum, Shh has roles to form and maintain fungiform papillae and taste buds, most likely via stage-specific autocrine and/or paracrine signaling, with epithelial/mesenchymal interactions. Neural crest cells also contribute to developing and postnatal lingual epithelium and mesenchyme, including taste papillae and taste buds. Further, Shh signaling in neural crest cells participates in patterning the tongue. In all, cells originating in several lingual tissue areas contribute to the stem and progenitor compartments that are active in forming and maintaining taste buds and papillae. Supported by NIH NIDCD Grant DC000456.

#24 **SYMPOSIUM: STEM AND PROGENITOR CELLS FOR TASTE BUDS — DEVELOPMENT AND RENEWAL**

In search of adult taste stem cells

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Recently, a great deal of progress has been made in identifying reliable markers for adult stem cells for many regenerative mammalian tissues. For instance, Lgr5 (leucine-rich repeat-containing G-protein coupled receptor 5) is a bona fide marker for adult stem cells in intestine, stomach, and hair follicle. In the small intestine of mice the Polycomb group protein Bmi1 marks another population of stem cells distinct from the Lgr5+ stem cells. Taste epithelium also regenerates constantly, yet the identity of adult taste stem cells remains elusive. In this study we set out to determine if Lgr5 and Bmi1 mark adult taste stem/progenitor cells. We found that Lgr5 is strongly expressed in cells at the bottom of trench areas at the base of circumvallate and foliate taste papillae and weakly expressed in the basal area of taste buds and that Lgr5-expressing cells in posterior tongue are a subset of K14-positive epithelial cells. Lineage-tracing experiments using an inducible Lgr5-Cre knock-in allele in combination with Rosa26-LacZ and Rosa26-tdTomato reporter strains showed that Lgr5-expressing cells gave rise to taste cells, perigemmal cells, along with self-renewing cells at the bottom of trench areas at the base of circumvallate and foliate papillae. Moreover, using subtype-specific taste markers, we found that Lgr5-expressing cell progeny include all three major types of adult taste cells. Our results indicate that Lgr5 may mark adult taste stem cells in the posterior portion of the tongue. In contrast, our lineage tracing experiments using Bmi1-Cre; Rosa26-LacZ showed that Bmi1 does not mark adult taste stem cells. Acknowledgements: This work was supported by NIH grants DC0101842 (P.J.), DK081421 (R.F.M.), DC003055 (R.F.M.), P30DC011735 (R.F.M) and a grant from the Commonwealth of Pennsylvania Department of Health (P.J.)

#25 **SYMPOSIUM: STEM AND PROGENITOR CELLS FOR TASTE BUDS — DEVELOPMENT AND RENEWAL**

Cell types in adult taste buds: distinct longevities and origins

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Mammalian taste buds are repopulated throughout adult life with new cells that are born in the basal epithelium immediately surrounding them. Taste buds contain several molecularly and functionally distinct classes of cells, but it is unclear whether each class is derived from a separate progenitor cell pool, and has similar longevity. Using high resolution confocal microscopy, and 4-color fluorescent labeling, we examined whether the previously described average life-time of taste bud cells applies to each of the cell types that make up the taste bud. After a single EdU injection to label newly born cells, we fitted exponential decay curves to the disappearance of labeled nuclei from each cell type. While sweet-, bitter- and umami-sensing Type 2 cells displayed a half-life of ≈8 days, sour-sensing neuron-like Type 3 cells were much longer-lived, with a half-life of over 22 days. Curiously, many post-mitotic cells had a prolonged quiescence inside taste buds before differentiating into mature taste cells. We also evaluated whether all taste cell types arise from a common pool of progenitor cells using lineage-tracing analyses in adult KERATIN14-cre/ERT;Rosa26-YFP mice. Non-taste keratinocytes were produced rapidly (within 2 days) from K14+ progenitors; Type I glial-like cells became YFP+ ≈10 days after induction, whereas Type II cells contained YFP+ cells only after ≈20 days. In stark contrast, Type III cells did not noticeably acquire the YFP lineage-label even 60 days after induction. Thus, while most cells of the taste bud arise from K14+ progenitors, the dynamics of their appearance suggests that several separate progenitor cell pools replenish adult taste buds during normal renewal. Supported by NIH/NIDCD R01DC6308

#26 **SYMPOSIUM: STEM AND PROGENITOR CELLS FOR TASTE BUDS — DEVELOPMENT AND RENEWAL**

Development and regeneration of the inner ear: Control of cell division and differentiation of sensory progenitors

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Loss of the sensory hair cells of the inner ear is the major cause of deafness and balance disorders. Hair cells are extremely sensitive to various environmental stressors such as ototoxic drugs noise, and aging. In mammals, the failure to regenerate these cells is complete, making hair cell loss a major global health problem. In contrast to the failure of regeneration in mammals, non-mammalian vertebrates can efficiently regenerate sensory hair cells through a combination of direct transdifferentiation

of the surrounding supporting cells, as well as by stimulated cell cycle reentry and subsequent differentiation of supporting cells into new functional hair cells and supporting cells. In spite of the failure of hair cell regeneration in mammals, recent work in the mouse has shown a latent regenerative potential for supporting cells to act as progenitors by both cell cycle reentry and transdifferentiation during the perinatal period, a potential that appears to be rapidly lost during early postnatal maturation. In this talk I will present recent findings on the molecular mechanisms that govern cell cycle reentry of otherwise postmitotic supporting cells, as well as mechanisms governing cell fate decisions between sensory hair cells, and the various supporting cell types in the developing and perinatal organ of Corti. I will also discuss the possibilities for future manipulation of supporting cells for the purpose of regeneration of lost sensory hair cells.

#27 SYMPOSIUM: STEM AND PROGENITOR CELLS FOR TASTE BUDS — DEVELOPMENT AND RENEWAL

Cellular basis of taste dysfunction following head and neck irradiation

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Taste dysfunction frequently occurs following radiotherapy for head and neck cancer. Importantly, patients with reduced taste function tend to lack appetite and eat far less, leading to weight loss and a significantly compromised quality of life. To determine the cellular targets contributing to taste dysfunction, we developed a mouse model of head and neck irradiation. We find that proliferating taste bud progenitor cells are immediate and direct targets of radiation damage. Specifically, head and neck irradiation results in: 1) increased apoptosis of progenitors within 24 hours of radiation exposure; and 2) a transient cessation in proliferation, lasting ~3 days. This latter effect results in an interrupted supply of new postmitotic taste cells to buds, and accounts for the subsequent reduction in differentiated taste cells seen at 1 week post-irradiation. We are now investigating the role of the novel protein kinase C delta isoform (PKC□) in irradiation-induced taste epithelial injury. PKC□ is a key regulator of irradiation-induced apoptosis, and suppression of PKC□ in vitro and genetic loss in vivo protects salivary gland cells from cell death. PKC□ is also implicated in maintenance of cell cycle arrest required for DNA repair in UV damaged human keratinocytes. Thus, we hypothesize that loss of PKC□ may protect taste progenitor cells from death, and/or promote their continued mitosis following irradiation injury. This model is supported by our pilot data, which suggest that, while PKC□ -/- mice possess normal taste epithelia, in response to irradiation, the taste bud progenitor population continues to proliferate. Thus, our studies point to PKC□ as a potential future target for interventional treatment for taste loss in head and neck cancer patients treated with radiotherapy. Supported by NIH/NIDCD R21DC011713 to LAB and MER, and P30DC004657 to D. Restrepo.

#28 PLATFORM PRESENTATIONS — POLAK YOUNG INVESTIGATOR AWARD WINNERS

Trace amine-associated receptors mediate behavioral aversion in mice

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The Trace Amine-Associated Receptors (TAARs) are a small set of evolutionarily conserved main olfactory receptors whose contribution to chemosensory function is not known. Our previous data show that a majority of the TAARs are mapped to a discrete group of highly sensitive amine-responsive glomeruli in the dorsal olfactory bulb of the mouse. Amines have been implicated as social cues and/or predator-derived chemosignals in rodents. We have used a combination of behavior and *in vivo* optical imaging to examine the functional consequences of genetically removing TAAR genes in mice. We find that deleting all 14 olfactory TAARs abolishes high sensitivity amine responses in the dorsal bulb and eliminates aversion that mice display to structurally diverse amines and to the volatiles of predator cat urine. Moreover, removing a single TAAR gene (*Taar4*) produces an odor-specific deficit in sensitivity and abolishes behavioral aversion to phenylethylamine—a chemical that is enriched in predator cat urine. Our data reveal that the TAARs mediate aversive responses in some behavioral contexts, and that individual TAAR genes contribute significantly to amine perception in mice. Acknowledgements: This work was supported by grants from NIH/NIDCD (R01DC009640), The Whitehall Foundation, and The Brain Research Foundation.

#29 PLATFORM PRESENTATIONS — POLAK YOUNG INVESTIGATOR AWARD WINNERS

Excess Wnt/β-catenin signaling in lingual epithelial progenitors drives production of type I taste cells at the expense of all other lingual epithelial cell fates

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In adult mice, taste cells are continually renewed from Keratin (K)14+ basal keratinocytes. As a population, K14+ basal cells

self renew, as well as produce post-mitotic cells which either differentiate into lingual epithelial cells (K13+), or enter buds and differentiate into type I, II and III taste cells (K8+). We previously showed that Wnt/β-catenin signaling is active in cells in and around taste buds of adult mice (Gaillard & Barlow, 2011), suggesting that this pathway may regulate several aspects of taste cell renewal. To test this idea, we used inducible Cre-lox technology to drive β-catenin gain of function (GOF) in K14+ basal keratinocytes throughout the tongue epithelium, including the fungiform and circumvallate papillae (CVP). In the CVP trenches, K13+ cells located between taste buds vanished in the GOF, and instead all cells within the CVP epithelium expressed K8. Using immunomarkers for each of the 3 taste cell types, we found that this expanded taste CVP epithelium comprised primarily NTPdase2+ type I cells, with little or no change in the numbers of type II and III cells. Likewise, in the anterior tongue, β-catenin GOF induced multiple K8+ cell clusters within fungiform papillae, as well as numerous ectopic K8+ cell clusters in non-taste epithelium; all of these cell clusters were exclusively NTPdase2+, and were devoid of expression of markers for type II and III taste cells. Our data indicate that excess Wnt/β-catenin signaling drives epithelial progenitors to produce daughter cells committed to a taste fate (K8+) at the expense of a non-taste fate (K13+), and moreover constrains these newly generated taste cells to a type I cell fate. We are now examining what cellular mechanisms are triggered by excess β-catenin, and how these changes in cell renewal result in the GOF phenotype. Acknowledgements: Supported by an American Heart Association fellowship to DG, NIH/NIDCD DC008373 and DC012383 to LAB, and DC004657 to D. Restrepo.

#30 PLATFORM PRESENTATIONS — POLAK YOUNG INVESTIGATOR AWARD WINNERS

Target-defined olfactory bulb output streams isolated using retrograde infection with recombinant viral vectors

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Recombinant viral vectors are an attractive tool for cell-type specific transgene expression, especially when Cre-dependent vectors are combined with Cre-expressing mouse lines. However, cell-type specific promoters do not always yield sufficient specificity for isolating functionally distinct neuronal populations. In the olfactory system mitral and tufted cells (MT) of the olfactory bulb (OB) constitute a heterogenous population with distinct dendritic organization, response properties and projections to olfactory cortex. Here, we demonstrate that by combining viral tools with retrograde infection via their axonal processes, MT cells can be defined by projection target. We injected Cre-dependent AAV vectors into various regions of olfactory cortex in Cdhr1-cre mice. Virus injection into anterior piriform cortex (PC) led to robust and widespread transgene expression in MT cells throughout the OB. To establish that expression patterns were due to retrograde infection we targeted additional olfactory cortical areas: injection into posterior PC or posterior cortical amygdala led to expression exclusively in mitral cells with lateral dendrites in the deep external plexiform layer, while injection into medial amygdala led to expression solely in mitral cells of the accessory olfactory bulb. Retrograde infection was effective using multiple transgenes including GCaMP and ChR2, allowing for optical imaging, optical control or optically-assisted electrophysiology of distinct OB output streams defined by their projection target. Retrograde infection was also effective for projection neurons in other brain regions. These results establish a valuable, easily-used tool for achieving combinatorial specificity in transgene expression to monitor and manipulate precisely-defined neuron populations in vivo. Acknowledgements: Supported by DFG and NIDCD

#31 PLATFORM PRESENTATIONS — POLAK YOUNG INVESTIGATOR AWARD WINNERS

Major contribution of Gαo-dependent vomeronasal chemoreception to sexual and reproductive behavior in female mice

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Optimal reproductive fitness is essential for the biological success and survival of species. The vomeronasal organ (VNO) is strongly implicated in the display of sexual and reproductive behaviors in female mice, yet the role that apical and basal vomeronasal neuron populations play in controlling these gender-specific behaviors remain largely unclear. To dissect neural pathways underlying these functions, we genetically inactivated the basal VNO layer using conditional, cell-specific ablation of the G protein Gαo. Female mice mutant for Gαo show severe alterations in mate recognition, mating, and reproduction. Male pheromonal cues fail to accelerate puberty onset and estrous synchronization in these mice. Gαo mutant females exhibit a striking reduction in sexual receptivity or lordosis behavior to males, but gender discrimination seems to be intact. These mice also show a loss in scent ownership recognition that requires a learned association with a nonvolatile ownership signal contained in the high molecular weight fraction of urine, and they show high pregnancy failure rates in the Bruce effect assay. These results indicate that sensory neurons of the Gαo-expressing vomeronasal subsystem, together with the receptors they express and the molecular cues they detect, control a diverse range of fundamental mating and reproductive behaviors in female mice. Acknowledgements: This work was supported by grants from the Deutsche Forschungsgemeinschaft to P.C. (CH 920/2-1), F.Z. (SFB 894) and T.L.-Z. (SFB 894), the Intramural Research Program of the NIH to L.B. (Project Z01 ES-101643), and the Volkswagen Foundation (to T.L.-Z.). E.J. was supported by the DFG-funded International Graduate Program GK1326. T.L.-Z. is a Lichtenberg Professor of the Volkswagen Foundation.

#32 PLATFORM PRESENTATIONS — POLAK YOUNG INVESTIGATOR AWARD WINNERS

Congruency matters: dual cortical processing of visual-olfactory integration

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Before ingestion, the visual appearance and odor of a food constitute its primary sensory inputs. Whether these distinct sensory events are perceived as one entity shapes their impact on subsequent food choice and possibly also food perception. We hypothesized that the degree of perceived concordance of the sensory inputs influences multisensory integration processes. To date, the behavioral consequences and brain mechanisms underlying these processes are poorly understood and were investigated with the present study. We used electrical neuroimaging analyses of the electroencephalographic (EEG) responses following olfactory-visual stimulation in humans. Stimuli were odor-image pairs presented as 100% congruent, 50% congruent and 100% incongruent. Participants rated the stimuli for congruence, pleasantness and intensity. As expected, concordant stimulus pairs were perceived as more congruent and as more pleasant than mixed and incongruent pairs. Waveform analysis yielded significant amplitude augmentation for congruent as compared to incongruent odor-image pairs between 120-200ms post stimulus onset. Source analysis revealed that the activation differences origin in visual cortex and left inferior temporal gyrus. Later differences were observed between 400-700ms in the parietal lobe, lateral frontal cortex and the bilateral insula. Concordance between olfactory-visual stimuli was associated with increased pleasantness and activation in unimodal visual and olfactory areas as well as in multimodal areas. The results suggest that cross-modal integration is a dynamic process regulated by both unisensory as well as higher order integration areas and that this process is modulated by learned associations and perceived congruence between the sensory inputs.

#33 PLATFORM PRESENTATIONS — POLAK YOUNG INVESTIGATOR AWARD WINNERS

Processing of hedonic and chemosensory features of taste in medial prefrontal and gustatory cortices

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The gustatory cortex (GC) is the main cortical recipient of taste-related signals, however it is not the only cortical area involved in processing taste. Upon elaborating gustatory signals, GC sends information to the orbitofrontal cortex (OFC) and the medial prefrontal cortex (mPFC). While considerable amount of work has been devoted to understanding how GC and OFC process different features of a gustatory experience, less is known regarding the role of mPFC. We investigated the involvement of mPFC in taste processing by comparing its responses to gustatory stimuli with those observed in GC. Eight rats were chronically implanted with movable bundles of electrodes in the ipsilateral mPFC and GC. Extracellular recordings were performed while 4 tastes were passively delivered through intraoral cannulae. The results showed significant taste related activity in mPFC. In comparison to GC, mPFC was less responsive to taste (49% of mPFC units responded to taste vs 75% in GC) and firing rates were lower in mPFC than GC. While taste selectivity was more pronounced in GC than mPFC, activity in mPFC appeared more strongly modulated by palatability. Results from a classification analysis revealed that units in GC decode taste quality more successfully than mPFC, and mPFC units encode tastes according to their palatability. Analysis of the time course of responses further revealed that, contrary to the GC where palatability coding occurs within the first 2 seconds following taste delivery, palatability coding in mPFC lasts for as long as 5 seconds. Furthermore, analysis of firing rates evoked by tastes revealed a bias toward aversive stimuli in mPFC. Altogether our results suggest a role of the mPFC in taste processing and more specifically point to mPFC as a cortical area involved in coding of palatability.
Acknowledgements: NIDCD Grant R01-DC010389

#34 SYMPOSIUM: NEW APPROACHES TO PHYSIOLOGY AND BEHAVIOR IN AWAKE RODENTS

New approaches to physiology and behavior in awake rodents

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As our understanding of neural circuitry grows more sophisticated, there is increasing interest in studying neuronal processing during volitional behavior in awake animals. At the same time, recent years have seen the emergence of many new techniques that allow unprecedented access to observe and control neural activity with spatiotemporal precision. These sensitive techniques can be difficult to implement and chemical stimulus control can be problematic in freely behaving animals. For these reasons, many labs are developing hybrid approaches in head-fixed preparations that fuse these new tools with rich behavioral paradigms in awake, behaving animals. The goal of this symposium will be to bring together investigators who are applying high resolution tools in awake animals to break new ground in our appreciation of the state modulation of chemosensory circuits and their governance of behavior.

#35 **SYMPOSIUM: NEW APPROACHES TO PHYSIOLOGY AND BEHAVIOR IN AWAKE RODENTS**

Dramatic state-dependency of the activity of granule cells in the mouse main olfactory bulb

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It is becoming increasingly clear that olfactory representations in the main olfactory bulb (MOB) are substantially reformatted in awake rodents. In addition to elevated rates and altered temporal structure in the spike discharge of mitral/tufted cells (MT), the wakeful state is marked by a fusion of sensory input-driven responses with activity that reflects attention, experience, and behavioral task contingencies. It seems likely that as a key target of many neuromodulatory systems and corticofugal feedback pathways, the extensive network of inhibitory MOB granule cells (GC) is instrumental in the state-dependent sculpting of MT activity patterns. Despite this predicted critical role, few published studies have demonstrably made electrophysiological recordings from these small cells. Moreover, none have been reported in awake animals. As a first step towards closing this gap, we recently developed reliable methods for recording and labeling GC in awake, head-fixed mice. Our preparation allows us to directly compare the activity and sensory responses of the same GC during wakefulness and inhalant anesthesia. Our data reveal that GC in awake mice are dramatically more spontaneously active, and exhibit stronger, more broadly-tuned sensory responses that include both increases and decreases in spike rate. Under either of two pharmacologically-distinct anesthetics, many of these cells emit very few spontaneous or stimulus-driven spikes. Those that have somewhat higher spontaneous rates still exhibit little response to odors. We are currently quantifying the variable respiratory coupling of GC in awake animals, and assessing the effects of stimulus novelty or familiarity on GC odor responses.

#36 **SYMPOSIUM: NEW APPROACHES TO PHYSIOLOGY AND BEHAVIOR IN AWAKE RODENTS**

Response properties of cortico-bulbar feedback and granule cells in awake head-fixed mice

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Sensory circuits integrate inputs from the environment, as well as feedback signals from higher brain regions, in a close loop manner. The interplay of feed-forward and feedback signals has been proposed to be fundamental for learning and memory recall. Though rich cortical feedback projections innervate the mouse olfactory bulb, to date, little is known about their contribution to olfactory processing. Cortico-bulbar feedback primarily targets the granule cells (GC), which form extensive dendro-dendritic synapses with the mitral/tufted cells. To examine how cortical feedback shapes processing in the bulb, we used genetically encoded calcium indicators (GCaMP3&5) and multiphoton imaging to monitor the odor evoked responses of feedback fibers and granule cells, in awake head-fixed mice. GCs and feedback fibers showed rich spontaneous activity and diverse excitatory and inhibitory odor responses. On average, to our stimulus panel (up to 30 odors), we observed 54% purely excitatory and only 17% purely inhibitory responses in the GCs, while the two response types were equally common in the feedback fibers. Interestingly, both GCs and feedback fibers, that showed spontaneous activity, were inhibited upon odor presentation, irrespective of stimulus identity. While inhibition of feedback fibers was sparse and odor specific, GCs showed both broad, and narrowly tuned inhibitory responses. Further, a significant fraction (~25%) of GCs exhibited excitatory OFF responses, independent of stimulus duration. We are currently investigating how response properties of GCs and feedback fibers are shaped by odor experience and during reinforcement learning. Additionally, we are employing pharmacological and optogenetic approaches to modulate the feedback fibers, while simultaneously monitoring granule cell activity.

#37 **SYMPOSIUM: NEW APPROACHES TO PHYSIOLOGY AND BEHAVIOR IN AWAKE RODENTS**

Odor-guided behaviors in head-restrained and freely-moving mice

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Olfaction plays a central role in guiding behavior in many animals, including the common laboratory mammalian models – rats and mice. There is a renewed excitement about studying the neural basis of such behaviors, which entails developing behavioral tasks under controlled conditions where neural activity can be recorded and manipulated. We have trained mice to perform odor tasks while their heads are restrained, which allows stable electrophysiological recordings, high-resolution optical imaging and optogenetic manipulation. In one such task, head-restrained mice can be trained to recognize target odorants embedded in unpredictable and variable background mixtures. We have also developed strategies to study odor-guided behaviors in freely moving animals, including spatial navigation. We will present a detailed analysis of these behaviors in our talk, and some initial efforts in recording and imaging neural activity under these conditions. Acknowledgements: R01DC011291

#38 SYMPOSIUM: NEW APPROACHES TO PHYSIOLOGY AND BEHAVIOR IN AWAKE RODENTS

Baseline states and odour evoked responses of mitral and tufted cells in the awake mouse

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Odour stimuli evoke activity patterns in the olfactory bulb, which are transformed in multiple steps by local microcircuits, before arriving to the cortex. Since inhibitory and excitatory synapses both exhibit short-term plasticity, the baseline activities and properties of odour-evoked responses strongly determine, how much individual neurons can influence information processing. Therefore, gaining an unbiased picture about the states of different neurons in the behaving animal is essential for understanding input transformation. We have performed blind whole-cell patch-clamp recordings in awake head-fixed mice to gain detailed and unbiased measurements of spontaneous and odour-evoked activity. Mitral and tufted cells (M & TCs) show great diversity in their baseline resting membrane potentials and spike rates. Both in awake and anesthetized animals, a large proportion (>33%) of cells have very low spontaneous firing rates (<1 Hz). In awake animals, M&TCs exhibit both inhibitory and excitatory subthreshold and suprathreshold odour-evoked responses. Strong, phasic excitatory responses can be observed in a subset of cells with hyperpolarized membrane potentials. TCs exhibit strong excitatory responses more frequently than MCs. Granule cells are characterized by exceedingly hyperpolarized resting membrane potentials (-66.3±3.4 mV), and the virtually complete lack of spontaneous spikes. In response to specific odours they show prolonged subthreshold and only rarely suprathreshold excitatory responses. This large heterogeneity in base firing rates and odour-evoked responses suggests that different subpopulations of principal neurons, defined by their internal states, have distinct roles in local processing and points to the importance of intracellular recording techniques for studying olfactory networks. Acknowledgements: Max-Planck-Society, Humboldt Foundation, DFG ExcellenzCluster CellNetworks, Bauer Foundation, Gottschalk Foundation, BMBF, DFG SPP 1392

#39 SYMPOSIUM: NEW APPROACHES TO PHYSIOLOGY AND BEHAVIOR IN AWAKE RODENTS

Integration of anticipatory and gustatory signals in the gustatory cortex of alert rats

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Neurons in the gustatory cortex (GC) do more than just encoding chemosensory signals coming from the thalamus. Evidence from behavioral and electrophysiological experiments indicates that GC neurons can also process affective information from limbic regions. The integration between sensory and limbic afferents is believed to explain why neural responses in GC of alert animals are plastic, multimodal and rich of reward-related information. My presentation will begin by reviewing evidence that activity in GC can be strongly affected by expectation and by auditory cues anticipating the general availability of taste. Data from different behavioral paradigms will be used to demonstrate that both classical and instrumental conditioning can result in robust anticipatory responses in the GC of restrained as well as freely moving animals. Experiments investigating the role of thalamic and limbic inputs in generating cue-responses will be presented. After a discussion of the system-level underpinnings for the integration of taste-coding and general expectation, I will show novel evidence that neurons in GC can also learn to encode specific expectation. Results from neural recordings in rats performing a two-cues auditory go/no-go task will be discussed. I will present data showing that cue responses are outcome specific and decrease significantly after partial extinction of cue-taste contingencies. Taste responses will be analyzed in neurons with different profiles of cue responsiveness and a relationship between responses to sucrose-anticipating cues and to sucrose itself will be established. Altogether our data will further establish the function of GC in integrating sensory and anticipatory signals and will provide a first analysis of the system-level mechanisms mediating this function. Acknowledgements: NIDCD R01-DC010389

#40 SYMPOSIUM: NEW APPROACHES TO PHYSIOLOGY AND BEHAVIOR IN AWAKE RODENTS

Differential synaptic control of mitral and tufted cell output pathways in the olfactory bulb

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Neurons in the gustatory cortex (GC) do more than just encoding chemosensory signals coming from the thalamus. Evidence from behavioral and electrophysiological experiments indicates that GC neurons can also process affective information from limbic regions. The integration between sensory and limbic afferents is believed to explain why neural responses in GC of alert animals are plastic, multimodal and rich of reward-related information. My presentation will begin by reviewing evidence that activity in GC can be strongly affected by expectation and by

auditory cues anticipating the general availability of taste. Data from different behavioral paradigms will be used to demonstrate that both classical and instrumental conditioning can result in robust anticipatory responses in the GC of restrained as well as freely moving animals. Experiments investigating the role of thalamic and limbic inputs in generating cue-responses will be presented. After a discussion of the system-level underpinnings for the integration of taste-coding and general expectation, I will show novel evidence that neurons in GC can also learn to encode specific expectation. Results from neural recordings in rats performing a two-cues auditory go/no-go task will be discussed. I will present data showing that cue responses are outcome specific and decrease significantly after partial extinction of cue-taste contingencies. Taste responses will be analyzed in neurons with different profiles of cue responsiveness and a relationship between responses to sucrose-anticipating cues and to sucrose itself will be established. Altogether our data will further establish the function of GC in integrating sensory and anticipatory signals and will provide a first analysis of the system-level mechanisms mediating this function. Acknowledgements: NIDCD R01-DC010389

#41 PLATFORM PRESENTATIONS: TASTE

Characterization of Testicular Bitter Taste Receptor-Mediated Signal Transduction

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Bitter taste receptors were initially isolated from mammalian taste bud cells in the oral cavity and are believed to function as a gatekeeper to prevent poisonous substances from ingestion. In addition to taste buds, however, these receptors have also been found in some extraoral tissues such as the respiratory epithelium and gastrointestinal tract. We detected the expression of these receptors in both human and murine testis, and found that male germ cells including spermatids and epididymal sperm can respond to bitter tasting substances by increasing intracellular calcium concentrations in a dose-dependent manner, and these calcium responses can be blocked by specific bitter blockers or the ablation of the G protein gustducin. Further characterization of these responses with pharmacological agents indicated that depletion of intracellular calcium stores with thapsigargin nearly abolished the calcium responses to the bitter compounds tested whereas the absence of the extracellular calcium did not affect the response amplitudes. Pretreatment of the cells with an adenylate cyclase inhibitor, MDL12,330A, also did not alter the response to caffeine. Thus our data suggested that testicular bitter taste receptors employ the G protein gustducin and calcium channels in the endoplasmic reticulum to mediate calcium responses to bitter tasting compounds. Further studies are in progress to elucidate the possible roles of these receptors in the reproductive system. Acknowledgements: This work was supported by National Institutes of Health Grant R01 DC007487 to L.H., by NIH-NIDCD Core Grant P30 DC011735 to R. Margolskee in support of Monell Core Facilities, and by National Science Foundation Equipment Grant DBI-0216310 to N. Rawson in support of Monell's Confocal Microscopy.

#42 PLATFORM PRESENTATIONS: TASTE

BDNF Maintains Adult Taste Innervation and Is Required For Taste Nerve Regeneration After Injury

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Brain derived neurotropic factor (BDNF) is required for the gustatory neuron survival and target innervation during development. However, whether BDNF has any function in the adult gustatory system or influences degeneration and regeneration after nerve injury is unclear. To address these issues, we inducibly removed BDNF in adulthood. In experimental animals, *Bdnf* expression decreased to 4% of control mice in the lingual epithelium and geniculate ganglion ($p<0.001$). We found no effect on taste bud morphology at 30 days following BDNF removal. However, 70 days following BDNF removal, P2X3-positive gustatory innervation to individual taste buds was reduced by nearly half ($p<0.001$) and both taste bud volume ($p<0.05$) and taste cell number decreased 30% ($p<0.01$). We unilaterally cut the chorda tympani nerve (CTX) two weeks after BDNF removal to determine whether degeneration and/or regeneration requires BDNF in adulthood. Two weeks after CTX, all P2X3-positive and most Tuj1-postive nerve innervation to the taste bud was gone ($p<0.001$) and taste bud number and size were decreased ($P<0.05$). There was no effect of BDNF removal on the degree of gustatory degeneration. However, preliminary data suggests that 60 days following CTX, much of the P2X3-positive and Tuj1-postive nerve innervation of control mice has returned and both taste bud number and taste bud size had increased by about 40% compared to two weeks post-CTX. However, mice lacking BDNF had no P2X3 labeled nerve fibers and few TuJ1-positvie nerve fibers returning to fungiform papillae. In addition, both taste bud number and taste bud size remained the same as two-weeks following CTX. These experiments demonstrate that BDNF is required for maintenance of taste innervation, and regeneration of gustatory nerve fibers in adulthood. Acknowledgements: NIH DC006938

#43 PLATFORM PRESENTATIONS: TASTE

Regulation of sugar habits by dorsolateral striatal circuits

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Despite the introduction of low-calorie sweeteners to the market, sugar consumption remains a major factor driving obesity rates throughout industrialized and emerging economies. Experimental psychologists named "habits" those inflexible behaviors, such as sugar intake, that persist despite their harmful consequences. The acquisition and expression of behavioral habits depend on the integrity of dopaminergic signaling in the lateral aspect of the dorsal striatum. Specifically, dopamine release in dorsolateral striatum is required for behavioral patterns to become insensitive to devaluation. We are investigating the role of dorsolateral striatal circuits in regulating intake of artificial sweeteners and sugars. We first determined whether animals exposed to daily access to sugar or artificial sweeteners

become resistant to reward devaluation, i.e. develop habit-like intake patterns. Adult mice were given 1h ad libitum access to sucralose paired to intra-gastric infusions of either glucose or sucralose. After a 14-days conditioning period, animals were tested after reward devaluation produced by a glucose intra-gastric preload. Mice challenged with glucose, but not with sucralose, maintained their daily intake after the preload, suggesting that sugar but not artificial sweeteners favor the formation of habits. Accordingly, intra-gastric glucose but not sucralose produced robust dopamine release in dorsolateral striatum, suggesting that sugar calories but not sweetness alone control dopamine efflux in this circuit. Current experiments involve evaluating whether stimulating dopamine signaling in dorsolateral striatum is sufficient for the formation of artificial sweetener habitual intake. Our data indicate that the dorsolateral striatum is critical for the inflexible nature associated with sugar intake. Acknowledgements: NIDCD grant DC009997

#44 PLATFORM PRESENTATIONS: TASTE

CALHM1 ion channel mediates purinergic neurotransmission of sweet, bitter and umami tastes

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Recognition of sweet, bitter and umami tastes requires the non-vesicular release from taste bud cells of adenosine 5'-triphosphate (ATP), which acts as a neurotransmitter to activate afferent neural gustatory pathways. However, how ATP is released to fulfill this function is not fully understood. Here we show that calcium homeostasis modulator 1 (CALHM1), a voltage-gated ion channel, is indispensable for taste stimuli-evoked ATP release from sweet-, bitter- and umami-sensing taste bud cells. Calhm1 knockout mice have severely impaired perceptions of sweet, bitter and umami compounds, whereas sour and salty taste recognition remains mostly normal. Calhm1 deficiency affects taste perception without interfering with taste cell development or integrity. CALHM1 is expressed specifically in sweet/bitter/umami-sensing type II taste bud cells. Its heterologous expression induces a novel ATP permeability that releases ATP from cells in response to manipulations that activate the CALHM1 ion channel. Knockout of Calhm1 strongly reduces voltage-gated currents in type II cells and taste-evoked ATP release from taste buds without affecting the excitability of taste cells to taste stimuli. Thus, CALHM1 is a voltage-gated ATP release channel required for sweet, bitter and umami taste perception.

#45 PLATFORM PRESENTATIONS: TASTE

Sonic Hedgehog Drives Nerve-Independent Formation of Adult Taste Buds

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Sonic hedgehog (Shh) is a key regulator of cell proliferation and differentiation. In the developing tongue, Shh patterns embryonic taste buds, but its role in maintenance of adult taste buds is unknown. We used an inducible, Cre-lox system, where K14CreER, when induced by tamoxifen, drives mosaic expression of Shh in taste and lingual basal keratinocytes. Unexpectedly, ectopic Shh expression induced ectopic taste bud formation in the lingual epithelium, a condition never encountered in wild type mice. Tongues examined for a general marker of taste cells, cytokeratin (K)8 at 1-4 weeks post-induction, had numerous K8+ cell clusters found external to fungiform papillae. Further, using markers of 3 differentiated taste cell types, we found type I, II and III taste cells in these ectopic cell clusters, revealing that these clusters were indeed taste buds. As taste bud differentiation and maintenance are nerve-dependent, we assessed if formation of ectopic buds was likewise nerve-dependent. Using P2X2, a marker of gustatory innervation, abundant neurites were present in fungiform buds, but were lacking from ectopic buds. However, using PGP9.5, a general marker of lingual nerve fibers, neurites were found in the vicinity of ectopic buds, although many ectopic buds were devoid of innervation. Therefore, we developed an unbiased, automated MATLAB script to quantify PGP9.5+ neurites in and around K8+ taste buds. We found no relationship between innervation and the presence of ectopic taste buds, controverting the general consensus that innervation is required for adult taste bud differentiation. Moreover, we demonstrate that Shh supplied via local epithelial cells is sufficient to drive differentiation of the entire taste bud cell complement in ectopic locations in a nerve-independent manner. Acknowledgements: NIH/NIDCD DC008373 and DC012383 to LAB, and DC004657 to D. Restrepo

#46 PLATFORM PRESENTATIONS: TASTE

Phenotypic Characterization of a Caudal to Rostral Intrasolitary Pathway

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Interactions between gustatory and visceral signals modulate ingestive behavior. The current study explored such interactions in the nucleus of the solitary tract (NST) where gustatory and visceral primary afferents terminate in largely separate rostral (rNST) and caudal (cNST) regions, respectively. Previous anterograde tracing suggests an intrasolitary projection from cNST to rNST (Karimnamazi et al.,'98) but the phenotypes of these connections have not been characterized. We made electrophysiologically–guided iontophoretic injections of the retrograde tracer, Fluoro-Gold (FG), into gustatory NST in wild-type and transgenic mice expressing EGFP under the control of the GAD67 promoter. Sections were immunostained for FG and tyrosine hydroxylase (TH) to identify catecholaminergic neurons or PHOX2b, a transcription factor that colocalizes with a subset of glutamatergic cells. Retrogradely–labeled cNST neurons extended caudal to obex. At a mid–postremal level, where several neuron types, including A2 catecholaminergic cells important in satiety are prominent, the intrasolitary pathway contained both PHOX2b/excitatory (~65$\pm$2.7%) and GAD67/inhibitory (27$\pm$2.5%) projections, with PHOX2b neurons located preferentially in the medial and intermediate NST and the GAD67 neurons distributed more laterally, including the ventral lateral NST. A smaller population (7$\pm$1.2%), presumably a subset of the PHOX2b cells, was double-labeled for FG and TH. Parallel experiments in rats showed a similar distribution of FG neurons labeled with dopamine beta hydroxylase implying that most TH–labeled neurons in mice are noradrenergic. In addition, *in vitro* recordings from rNST demonstrate that norepinephrine has a suppressive effect on solitary tract–evoked responses, suggesting a functional role for the A2 projection.
Acknowledgements: Supported by DC00416 & T32DE014320

#47 PLATFORM PRESENTATIONS: TASTE

Longitudinal analysis of 40% calorie restriction on rat taste bud morphology and expression of sweet taste modulators

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Taste perception is strongly associated with body weight and metabolic state. Caloric restriction (CR) is a well-characterized intervention that reduces body weight and improves metabolic function. In this study, we performed a longitudinal analysis to determine the effects of 40% CR on rat taste bud morphology and expression of sweet taste modulators. Immunohistochemical analyses of the effects of 40% CR on taste buds were made with 5-, 17- and 30-month old male Fisher 344 rats. No significant effects of 40% CR on taste bud size and number of taste cells per taste bud were noted. However, 30-month old rats (both ad libitum (AL) and calorie restriction (CR) groups) possessed smaller taste bud size and fewer taste cells per bud than 5- (significant) or 17- (non-significant) month old CR or AL rats. There was no significant effect of 40% CR or aging on Type 1 (NTPDase 2), Type 2 (PLC-beta 2), or Type 3 (NCAM) taste cells marker expression. In contrast, both 40% CR and AL 30-month old rats demonstrated significantly lower Type 4 (Shh) taste cell marker expression. We found that α-gustducin expression was significantly higher in 5-month old 40% CR rats compared to AL, with similar trends for T1r3 and glucagon-like peptide 1 (GLP-1) expression. However, T1r3, GLP-1 and α-gustducin expression were decreased in 30-month old 40% CR rats compared to age-matched AL rats. Leptin receptor expression was significantly higher in 17- and 30-month old 40% CR rats, compared to age-matched AL rats. Our findings suggest that short- and long-term CR elicit differential responses on rat taste bud morphology and sweet taste modulator expression. This is likely due to long- and short-term calorie intake and metabolic homeostatic adaptations to the CR regimen.
Acknowledgements: This work was supported entirely by the Intramural Research Program of the National Institute on Aging, National Institutes of Health.

#48 SYMPOSIUM: EXPERIENCE DRIVEN PLASTICITY OF THE OLFACTORY SYSTEM

Experience Driven Plasticity of the Olfactory System

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The olfactory system has been thoroughly investigated during several decades. A number of its functions have been well described such as i) the olfactory transduction pathways; ii) the central odor processing and cerebral and neural networks; iii) the mechanisms of neurogenesis and synaptic plasticity. The olfactory system reveals itself as a flexible sensory processing system. While the implication of experience and internal state on olfactory detection and processing has been explored, some points remain unclear: whether experience can modulate specific populations of olfactory sensory neurons (OSNs) and olfactory bulb (OB) input and output maps. New tools were recently developed to analyze the plasticity of the olfactory system such as genetic labeling of specific population of OSNs (i.e. expressing specific OR), molecular biology tools (qRT-PCR), genetic labeling for synaptic transmission imaging and *in vivo* imaging. This symposium focuses on the dynamic nature of olfactory processing: the effects of experience on how odors are processed from olfactory sensory neurons to higher-order structures and how recent techniques are used to investigate these questions in different structures and models. In mice, we will discuss: i) the effects of olfactory experience on specific OSNs populations and synaptic transmission; ii) the effects of emotional experience on OSNs function; ii) the importance of the balance between activity, regeneration and remodeling for OB plasticity; iii) the use of long-term imaging of odor representations in awake mice to explore olfactory plasticity. Finally, plasticity induced by

olfactory experience on behavior and brain in an Insect model will be presented. We aim to present the state of the art about the olfactory system as a flexible, adaptable and plastic system.

#49 **SYMPOSIUM: EXPERIENCE DRIVEN PLASTICITY OF THE OLFACTORY SYSTEM**

Postnatal Odorant Exposure Induces Peripheral Olfactory Plasticity

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Olfactory sensory neurons (OSNs) form an interface between the environment and the brain, converting chemical information (odorants) into electrical signals and sending these signals to the brain. Little is known about the consequences of long term odorant exposure on OSNs. Our goal is to understand the anatomical, molecular and physiological effects of odorant exposure at the cellular level and more precisely in the context of an early postnatal olfactory exposure. We focus our work on specific populations of OSNs expressing particular ORs using gene-targeted mice. MOR23-GFP mice were exposed daily to Lyral and anatomical, molecular and physiological properties of these neurons were analyzed. The density of MOR23 neurons decreased after odorant exposure while the level of mRNA for the receptor remained stable at the entire mucosa level. To investigate molecular changes within individual OSNs, mRNA levels for olfactory signaling pathway components were quantitatively analyzed using qPCR on GFP-containing neurons (7 per mouse). The levels of mRNAs for CNGA2, PDE1C and MOR23 olfactory receptor were higher in exposed OSNs compared to control. Using patch-clamp recordings on the dendritic knobs of MOR23 neurons in an intact preparation we observed that exposed OSNs displayed a lower detection threshold compared to control OSNs while the dynamic range of the dose-response was broader. Responses of exposed neurons were also faster and shorter than the responses of control neurons. Postnatal odorant exposure induces molecular and physiological plasticity in individual MOR23 neurons. Taken together, our data suggest that the olfactory epithelium presents deep anatomical, molecular and functional changes when chronically exposed to odorant molecules in early stage of life. Acknowledgements: Funding was provided by CNRS (ATIP grant), by Conseil Régional de Bourgogne (FABER and PARI grants), and by Université de Bourgogne (BQR program).

#50 **SYMPOSIUM: EXPERIENCE DRIVEN PLASTICITY OF THE OLFACTORY SYSTEM**

Altered olfactory sensory neuron physiology following odor exposure or olfactory fear conditioning *in vivo*

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Experience-dependent plasticity is increasingly understood to occur throughout adulthood in mammalian sensory systems. This talk will present data from experiments that used optical imaging to longitudinally assess the effects of odorant exposure and emotional learning on the physiology of olfactory sensory neurons (OSNs) *in vivo* in individual adult mice. In 1 experiment, mice expressing the fluorescent exocytosis indicator synaptopHluorin in mature OSNs underwent a baseline imaging session in which a chronic cranial window was implanted in the skull overlying the olfactory bulbs and the OSN synaptic output into olfactory bulb glomeruli was visualized during the presentation of a panel of 4 odorants (2 esters, 1 aldehyde, and 1 ketone). Mice then spent a week in either an odorant-exposure chamber in which 1 of the esters was presented repeatedly with a 4 hour duty cycle or in a control chamber. After exposure, the exposed ester and the control ester both evoked less OSN synaptic output into fewer glomeruli than prior to exposure, while aldehyde- and ketone-evoked responses were unchanged. In a separate experiment, mice underwent a similar baseline imaging session but were then differentially fear conditioned to associate 1 ester (the CS+) with shock while the other ester (the CS-) was presented without shock. In a post-conditioning imaging session the glomeruli that received OSN input driven by the CS+ received larger synaptic inputs from OSNs, while responses to the CS- and non-presented control odorants were unchanged. Control mice that experienced only odors or only shocks between imaging sessions exhibited no changes in the response to any odorant. These data provide surprising evidence that environmental changes and emotional learning can change how OSNs respond to olfactory stimuli. Acknowledgements: This work was supported by the National Institute on Deafness and Other Communication Disorders (R00 DC009442 to JPM).

#51 **SYMPOSIUM: EXPERIENCE DRIVEN PLASTICITY OF THE OLFACTORY SYSTEM**

Understanding Plasticity in the Olfactory Intrabulbar Map

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In the mammalian olfactory system sensory neurons project their axons to the surface in the olfactory bulb generating a pair of glomerular maps that reflect odorant receptor identity. These maps are further connected through a set of reciprocal intrabulbar projections that are mediated by tufted cells that specifically link iso-functional odor columns to produce a second order map called the intrabulbar map. We have shown that intrabulbar projections are established postnatally and undergo continuously refinement through an activity dependent process that has no critical period. Here we present that both loss of olfactory sensory input and broad odorant stimulation are capable of disrupting the intrabulbar map specificity, while re-introduction of normal activity restores the map to proper order. We also reveal that the regenerating interneurons are central to intrabulbar circuit plasticity and that proper connectivity depends specifically upon new neurons from the rostral migratory stream. Together these data illustrate that olfactory bulb plasticity is a balance between activity, regeneration and remodeling. Acknowledgements: National Institute of Neurological Disorders and Stroke, Intramural Research Program.

#52 **SYMPOSIUM: EXPERIENCE DRIVEN PLASTICITY OF THE OLFACTORY SYSTEM**

Long-term imaging of odor representations in awake mice

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How are sensory representations in the brain influenced by the state of an animal? Here we use chronic two-photon calcium imaging to explore how wakefulness and experience shape odor representations in the mouse olfactory bulb. Comparing the awake and anesthetized state, we show that wakefulness greatly enhances the activity of inhibitory granule cells and makes principal mitral cell odor responses more sparse and temporally dynamic. In awake mice, brief repeated odor experience leads to a gradual and long-lasting (months) weakening of mitral cell odor representations. This mitral cell plasticity is odor specific, recovers gradually over months, and can be repeated with different odors. Furthermore, the expression of this experience-dependent plasticity is prevented by anesthesia. Together, our results demonstrate the dynamic nature of mitral cell odor representations in awake animals, which is constantly shaped by recent odor experience.

#53 **SYMPOSIUM: EXPERIENCE DRIVEN PLASTICITY OF THE OLFACTORY SYSTEM**

Olfactory Experience Shapes Insect Olfactory Centres

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Insects provide excellent models to study how neural networks dedicated to olfactory processing are formed during development, and how they work in the adult. However, their organisation is not fixed once development is achieved. On the contrary, as in vertebrates, the connectivity and functional organisation of insect olfactory systems are not fixed: they exhibit clear plastic properties, as shown in various species over the recent years. In our work, we have been focusing on the plastic changes affecting the anatomy of the olfactory centres as a consequence of olfactory experience, be it the mere exposure to environmental odorants or associative learning and memory. In particular, we have been looking for structural rearrangements in two main olfactory centres known for their role in olfactory learning and memory in the insect brain: the antennal lobes and the mushroom bodies. The modular organization of these two neuropils allows quantifying the changes affecting their structure in the brains of animals submitted to different treatments. By doing so, and by focusing mostly on the honeybee (*Apis mellifera*) as a model species, we have been able to show that the formation of long-term memories of previous olfactory experience is associated with structural modifications in insect olfactory networks. Interestingly, such modifications vary with the nature of the experience undergone by the animal, and may be considered as supports of olfactory memories. Thus, they are likely to contribute to the acquisition and retention of behavioural responses adapted to changing environments.

#53.5 **CLINICAL LUNCHEON: TASTE RECEPTORS IN GUT AND PANCREAS REGULATE ENDOCRINE FUNCTION**

Robert F. Margolskee
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Many of the receptors and downstream signalling proteins involved in taste detection and transduction are expressed also in intestinal and pancreatic endocrine cells where they underlie certain chemosensory responses. Intestinal endocrine cells express T1r taste receptors, the taste G-protein gustducin, and several other taste transduction elements. So too do pancreatic islet endocrine cells. Knockout mice lacking alpha-gustducin or the sweet taste receptor subunit T1r3 have deficiencies in intestinal secretion of glucagon-like peptide-1 (GLP-1) and in the regulation of plasma levels of insulin and glucose. Glucose-dependent insulin release from mouse pancreatic islets ex vivo is stimulated by sucralose and other sweeteners. Islets from T1r3 knockout mice release insulin normally in response to glucose, but show no enhanced release of insulin in response to non-caloric sweeteners. Thus, there appear to be two mechanisms

for regulating insulin release from pancreas, one dependent on glucose, glucose transporters and glucokinase, and another for sweeteners that involves T1r3 and other taste proteins. Only limited studies with humans have been done in this area, but it seems likely that "taste" signalling proteins in human gut and pancreas also contribute to chemosensory responses in gut and pancreas to regulate glucose homeostasis.

#54 **SYMPOSIUM: THE NEW 'FACES' OF CHEMOSENSATION — UTILIZING CHEMOSENSORY SIGNALING PATHWAYS OUTSIDE THE CANONICAL CHEMOSENSORY ORGANS**

Symposium: The New 'Faces' of Chemosensation – Utilizing Chemosensory Signaling Pathways Outside the Canonical Chemosensory Organs

Yehuda Ben-Shahar[1,2]

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In recent years, several exciting studies indicated that canonical mammalian chemosensory signaling pathways are also likely to function outside the canonical chemosensory organs (taste and olfaction). These findings significantly expand our field of view in terms of what constitutes a chemosensory organ, and suggest that cell-autonomous chemoreception, independent of the nervous system, is likely playing an important role in health and disease, which includes digestive, respiratory, and reproductive functions. This symposium will present the current state of knowledge about the possible extra-sensory functions of 'taste' and 'olfaction' signaling molecules in non-sensory tissues and cells.

#55 **SYMPOSIUM: THE NEW 'FACES' OF CHEMOSENSATION — UTILIZING CHEMOSENSORY SIGNALING PATHWAYS OUTSIDE THE CANONICAL CHEMOSENSORY ORGANS**

Human Pulmonary Neuroendocrine Cells are Olfactory Sentinels

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Previous work indicated that mammalian pulmonary ciliated epithelial cells act as chemosensory cells to non-volatile stimuli. Whether human airways can also detect volatiles is not known. However, human pulmonary diseases such as asthma have been linked to increased sensitivity of the airways to various volatile insults. We have identified several expressed canonical olfactory receptors in human primary airway epithelia. Immunohistochemistry on lung sections and primary airway cultures to identified candidate olfactory sensory cells in human airways, which can respond to volatiles in culture. Using several well-established markers for various pulmonary epithelial cell types we identified the olfactory cells as pulmonary neuroendocrine cells (PNEC). In humans, PNECs are morphologically distinct cells of unknown function. We found that human PNECs express members of the olfactory receptor family and are anatomically positioned to respond to inhaled volatile chemicals. Further, human olfactory PNECs showed high levels of vesicular 5-HT and the peptide hormone CGRP, further establishing the pulmonary neuroendocrine system as olfactory sensory sentinels. Apical exposure of primary human airway cultures to volatile chemicals led to the release of the neuroendocrine content of PNECs, indicating that adult human PNECs could act as olfactory sensory cells. Since pulmonary tissues express diverse serotonin and peptide receptors, these data indicate that human airway epithelia evolved a specialized group of cells that can act autonomously in response to volatile chemical insults. These cells may represent the missing cellular and physiological links between the exposure to environmental volatiles and airway hypersensitivity observed in some pulmonary diseases. Acknowledgements: NIH NIDCD R03DC010244 and the Children's Discovery Institute (St. Louis)

#56 **SYMPOSIUM: THE NEW 'FACES' OF CHEMOSENSATION — UTILIZING CHEMOSENSORY SIGNALING PATHWAYS OUTSIDE THE CANONICAL CHEMOSENSORY ORGANS**

Bitter Taste Receptors on Airway Smooth Muscle: a target for novel bronchodilators

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There is an unmet need for treatments of the airway constriction that occurs in asthma. Currently, beta-agonists are the only class of direct bronchodilators that are in use. We unexpectedly found T2Rs (particularly subtypes 10, 14, 31) expressed on human airway smooth muscle (ASM). Activation by T2R agonists causes significant and reversible ASM relaxation in human and mouse airways, isolated human ASM cells studied by magnetic twisting cytometry and Fourier transform traction maps, and in mice in vivo. Signaling was sensitive to inhibitors of betagamma, PLC, and the IP3 receptor, and was associated with membrane hyperpolarization and an increase in SR-released intracellular [Ca2+] within a sequestered pool restricted to the cell surface. One channel that appears to be involved is BKca, but there may be others. In the ovalbumin-sensitized mouse model of asthma, the inhaled T2R agonist quinine was much more efficacious than the inhaled beta agonist albuterol in reversing airflow obstruction. Given the large number of known bitter tastants, there is an opportunity to discover non-toxic T2R agonists for inhalation for the treatment of obstructive lung disease.

#57 **SYMPOSIUM: THE NEW 'FACES' OF CHEMOSENSATION — UTILIZING CHEMOSENSORY SIGNALING PATHWAYS OUTSIDE THE CANONICAL CHEMOSENSORY ORGANS**

Genetics of the bitter taste receptor T2R38 underlie susceptibility to upper respiratory infection

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Innate and adaptive defense mechanisms protect the respiratory system from attack by microbes. Here, I describe our recent studies that demonstrate that the bitter taste receptor T2R38 is expressed in the human upper respiratory epithelium and is activated by acyl-homoserine lactone quorum sensing molecules secreted by *Pseudomonas aeruginosa* and other gram-negative bacteria. T2R38 regulates human upper airway innate defenses through nitric oxide production, resulting in stimulation of mucociliary clearance and direct antibacterial effects. Moreover, common polymorphisms of the *TAS2R38* gene are linked to significant differences in the ability of upper respiratory cells to clear and kill bacteria. Lastly, *TAS2R38* genotype correlates with human sinonasal gram-negative bacterial infection. These data suggest that T2R38 is an upper airway sentinel in innate defense, and that genetic variation that contributes to human individual differences in ability to taste phenylcarbamide (PTC) and related molecules also contributes to individual differences in susceptibility to respiratory infection. Acknowledgements: P30DC011735 R01DC004698 P50DC000214 R01DC010842

#58 **SYMPOSIUM: THE NEW 'FACES' OF CHEMOSENSATION — UTILIZING CHEMOSENSORY SIGNALING PATHWAYS OUTSIDE THE CANONICAL CHEMOSENSORY ORGANS**

Detection Of Irritants And Bacterial Metabolites Via The Taste Transduction Cascade In Solitary Chemosensory Cells Of The Nasal Cavity

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Airways are continually assaulted by harmful compounds carried on the incoming airstream and by the potentially pathogenic bacterial populations. We have shown that the nasal epithelium of rodents houses a population of trigeminally-innervated solitary chemosensory cells (SCCs) that express T2R taste receptors along with their downstream signaling components crucial for detection and response to these deleterious agents. SCCs are distributed across much of the nasal respiratory epithelium in rodents, but are especially concentrated along curved surfaces facing major airway conduits. In the upper respiratory passageways, the SCCs express nearly all T2Rs tested as well as some T1R family members. Downstream signaling components also are expressed by SCCs including: gustducin, PLCß2 and TrpM5. Functionally, SCCs respond rapidly to bitter ligands (e.g. denatonium 10mM) as well as bacterial signaling molecules including the acylhomoserine lactones produced as quorum sensing molecules by *Pseudomonas* species. Activation of the SCCs by these compounds evokes neurally-mediated protective reflexes, involving both apnea and local neurogenic inflammation. These responses are absent in both gustducin and TrpM5 knockout mice implicating the taste transduction cascade as a crucial component of responses to these substances. Moreover, the local inflammatory responses were absent after chemical ablation of the nociceptive fibers of the trigeminal nerve showing the necessity for innervation. More recently we have tested the possibility that similar SCCs are present in the human nose and now report (S. Cooper AChemS 2013) the presence of elongate TrpM5+ microvillous cells within the sinonasal epithelium in humans. Whether similar SCCs underlie epithelial defense systems in humans remains to be determined. Acknowledgements: Supported by NIDCD grants to T. Finger, SC Kinnamon (RO1 DC009820), M Tizzano (R03 DC012413) and the Rocky Mountain Taste & Smell Center (P30 DC04657)

#59 **SYMPOSIUM: THE NEW 'FACES' OF CHEMOSENSATION — UTILIZING CHEMOSENSORY SIGNALING PATHWAYS OUTSIDE THE CANONICAL CHEMOSENSORY ORGANS**

Block of taste genes leads to male sterility

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The male infertility rate in the developing world is increasing. About 7% of men are infertile for unknown reasons, while having normal hormone levels. We found that two gene products (T1R3 and gustducin) originally found in taste chemosensation are expressed in haploid spermatids and their absence or block leads to male sterility. The pathology shows an arrest in spermatid development with numerous giant and exfoliated cells in testicular tubules, oligospermia and immotile sperm. To study this phenomenon we produced a mouse model expressing a humanized form of T1R3 that can be inhibited by human-specific inhibitors. Some of these inhibitors are phenoxy compounds developed into common medications and agricultural chemicals. A very effective, yet reversible, sterility is achieved by treatment with the phenoxy compound clofibrate in this model with humanized T1R3 receptor in the background of gustducin null allele. Because both T1R3 and gustducin affect cAMP levels, we hypothesize that their absence impairs function of CREM (cAMP response modulator protein) a transcriptional master gene indispensable for spermatid development and EPAC (exchange protein activated by cAMP) a Rap 1 activator required

for cell adhesion. We further hypothesize that even low levels of chemicals and/or medications acting on T1R3 and gustducin, possibly in combination with other drugs, can negatively affect human male fertility. Acknowledgements: R21 DC007399 - NIH/NIDCD, R01 DC003155 - NIH/NIDCD, P30DC011735 - NIH/NIDCD.

 # 60 **IFF LECTURE: BITTER TASTE IN MICE AND MAN**

Bitter Taste in Mice and Man

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Bitterness is elicited by numerous structurally diverse molecules which usually act as repellents allowing us to avoid intake of harmful food. However, we adapt to and even prefer the bitterness of some foods and beverages. To elucidate these phenomena my laboratory investigates the receptors and cells for bitter tasting compounds in man and mice.

Functional assays with >100 chemicals demonstrate similar molecular receptive ranges for the repertoires of murine and human Tas2r bitter taste receptors even though the number of cognate compounds discovered for the human TAS2Rs was larger. This is surprising since the mouse genome encodes 30% more bitter receptors than the human genome does. Notably, the two species usually detect the same compounds with non-orthologous Tas2rs. Both species possess generalists, moderately tuned Tas2rs and specialists according to their number of cognate bitter compounds. However, a larger fraction of specialists occurs in mice, proposing that the luxury of having specific receptors for solitary bitter compounds in a species is supported by a greater number of TAS2R genes.

Genetic labeling and in situ hybridization experiments visualized the populations of bitter-sensing cells in mice and man. They express the complete repertoires of Tas2r genes but individual cells express only limited subsets. This is supported by genetic ablation in mice of the cells for Tas2r131 which extinguished only ~50% of the bitter cell population. Oral administration of bitter compounds to mice excites specifically 200-400 neurons in the gustatory part of the nucleus of the solitary tract as indicated by induction of immediate early gene. These gustatory neurons respond differently to different oral bitter stimuli. Finally, we found that mice without Tas2r131 cells avoid several bitter compounds less than controls, whereas they are indistinguishable from controls in their avoidance of denatonium benzoate.

Our data demonstrate that bitter sensing cells and their gustatory target neurons are functionally distinct forming the basis for variable behavioral responses to different bitter chemicals which could be of relevance for ingestive behavior.

#P1 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Meteorological Vaticination through Phantosmia: A Case Study

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Introduction: Linkage of weather to chemosensory hallucinations has heretofore not been reported. Methods: Case Study: A 64 yo M presents with five years of intermittent noxious skunk-onion excrement phantosmia, lasting for hours. If severe, he tastes the same odor. It is exacerbated by coughing and nasal congestion, and alleviated with sleep, nasal irrigation, alprazolam, occluding nostrils, assuming Moffitt's position, snorting salt water, blowing nose, and holding breath. When eating or sniffing, the actual flavors replace the phantosmia. Since onset, he noted the intensity and frequency of the phantosmia forecasted the weather. Two hours before a storm, the phantosmia intensifies from a level 0 to a 7-10, which persists through the entire thunderstorm. Twenty years prior, he noted the ability to forecast the weather, based on pain in a torn meniscus, which vanished after surgical repair. Results: Olfactory testing revealed hyposmia: QSIT 1; ETOH Sniff Test 3cm; BSIT 8; PST 2; Odor Memory Test: 2-10 sec., 2-30 sec., 0-60 sec.; UPSIT – 27 R, 8 L, Sniffin' Sticks – Threshold: L <1, R <1, dirhinous <1, Discrimination: L 9, R 8, dirhinous 10; Identification: L 8, R 6, dirhinous 6; Sniff Magnitude Test: 1.02 – 1.12 (Anosmia); PEA Testing: L= - 5.0 R > -2.0. Conclusion: Decrease in barometric pressure may precipitate phantosmic synestesthia or reduces already hyposmic olfactory ability, serving to disinhibit phantosmia. Atmospheric changes may induce contractions on a scarred olfactory nerve, heightening ectopic discharge. Menacing weather may impair mood, enhancing awareness of interoceptive bodily symptoms and somatic sensory amplification. Misattribution error may have occurred by expectation effect or selective attention. This is the first reported case of weather-induced exacerbation of phantosmia.

#P2 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

The Effects of Aroma of Baked Cinnamon Bun on Stability

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Objectives: Dizziness or instability affects almost 70 million Americans, and is of multimodal origin. Odors can influence many physiological systems including, the automatic nervous system, nociceptive, visual, and somesthetic; all of which play a role in dizziness. No studies have demonstrated the effects of odors on dizziness. This study addresses if a hedonically pleasant odor, baked cinnamon bun (BCB), can impact stability. Methods: 11 normosmic (3/3 Q-SIT) subjects, aged 20-58, 3 males, 8 females, underwent a test of stability while wearing blank surgical masks or surgical masks impregnated with BCB (IFF), in a counter balanced order. Subjects completed the Single Leg Balance Test using the Nintendo Wii Fit™ software in combination with the Nintendo Balance Board™ as per published protocol. Subjects were tested on the non-dominant leg (the opposite of the leg used to kick a ball). Results: 10 subjects reported positive hedonics to the odor of BCB. Order of presentation had no effect on the outcome (p=.96). Gender does have an effect on the outcome, with higher stability percentage in females (66.7 vs. 65.6, p=.0009). However, the BCB-versus-blank effect is not different between men and women. Stability percentage is significantly higher using BCB compared to blank; Stability percentage 67% using BCB, 60% with un-odorized mask, with each person serving as their own control (p=.02). Conclusions: BCB odor improved balance significantly in our healthy test subjects. The use of hedonically favorable BCB aroma may have utility in treatment for those who suffer from dizziness or in stability. Further testing on those suffering from dizziness is warranted

#P3 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Superficial Siderosis-Induced Anosmia

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OBJECTIVE: Superficial siderosis, a rare condition that results from the deposition of hemosiderin in the central nervous system, has been reported to cause anosmia in 17%. METHODS: A 49-year old female patient with superficial siderosis and anosmia is presented. RESULTS: Chemosensory function was evaluated using ETOH Sniff Test; Quick Smell Identification Test; Brief Smell Identification Test; Pocket Smell Test; University of Pennsylvania Smell Identification Test, Extended Sniffin' Stick Tests of threshold, discrimination and identification; Suprathreshold Amyl Acetate Odor Hedonic and Intensity Tests, Monorhinous Phenylethyl Alcohol Smell Threshold Test; Retronasal Smell Testing, Accusens Taste Tests, Taste Quadrant Testing, and PROP paper. Abnormalities were noted in mono and dirhinous detection, discrimination, identification, hedonics, intensity perception, retronasal smell, taste threshold to HCl, and taste quadrant to sucrose and quinine. Besides anosmia and hypogeusia, she had mild sensorineural hearing loss and chronic bifrontal throbbing headache, which was diagnosed as pseudotumor cerebri. Brain MRI revealed hemosiderin deposition in the bilateral cerebellar hemispheres, left Sylvian fissure, and the anterior poles of bilateral temporal lobes. Lumbar puncture revealed increased

pressure and blood in cerebrospinal fluid. CONCLUSIONS: The chemosensory loss of the patient is postulated to be due to deposition of hemosiderin on the olfactory nerve. In superficial siderosis, anosmia or hyposmia is common, but olfactory function testing is rarely undertaken. Earlier case reports of superficial siderosis have not described detailed chemosensory tests. This is the first report of superficial siderosis-induced chemosensory deficit with presentation of a set of objective chemosensory testings.

#P4 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Postviral Hyposmia with Transient Improvement by Spontaneous Yawning

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Objective: To describe a patient with hyposmia whose olfactory ability returns upon yawning. Method: 61yo male, three years ago noted nasal congestion, followed by loss of smell and taste. Sinus CT showed opacification of the ethmoidal and an air-fluid level in the right maxillary sinus. After treatment, sinus CT, MRI, and fiberoptic endoscopy were normal, but smell ability remained at 5%. He is able to smell flowers and gasoline if held close. Immediately after yawning he was able to smell for a second. With small yawns 20% returns; 100% with large yawns. Two years ago transient phantosmias began of rubber or chemicals. His taste is 1-2%. He can taste Chinese mustard and red pepper. Results: Chemosensory testing indicated hyposmia and hypogeusia. Q-SIT 2; Sniff Magnitude with Sniff Magnitude Ratio of .87; Alcohol Sniff Test 11 cm; Sniffin' Stick Threshold L <1, R <1, bilateral <1; Discrimination L 4, R 4, bilateral 6; Identification L 4, R 5, bilateral 7; UPSIT R 19, L 18; Odor Memory Test 10 sec 3, 30 sec 4, 60 sec 2, total 9/12; Smell Threshold with PEA L > - 2.0, R > - 2.0; Suprathreshold Amyl Acetate Odor Intensity - normal at high intensity; Suprathreshold Amyl Acetate Odor Hedonics - normal. Spatial Taste Test - weakness on the whole tongue and palate to NaCL and Sucrose, right anterior and posterior tongue to citric acid and quinine hydrochloride. PROP disc - normal. Fungiform papillae L 22, R 18. Retronasal smell: with nose clip 1/10, without nose clip 4/10. Dirhinous PEA Threshold Testing -2.5; After Polite Yawning Technique > -2.0; After Induced natural yawn > -2.0. Conclusion: Yawning may improve olfaction by enhancing nasal airflow. The polite yawning technique should be considered to be part of the evaluation in those who complain of chemosensory dysfunction.

#P5 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Tests of Retronasal Smell in Children: Which Flavored Jelly Bean Works Best?

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Objective: In 13 adults, Mozell et al (1969) found flavor dependent effects of different foods of retronasal smell on identification, but did not address intensity. Engen (1982) posited that the olfactory role in identification differs from intensity assessments. We looked to determine, in children, the retronasal component of intensity of flavored jelly beans. Methods: Forty two, 12 or 13 year olds, were screened with the Brief Smell Identification test. Twenty five (17 girls, 8 boys) scored 3/3 and underwent an assessment of intensity, on a 10 point visual analog scale, with and without nose clips, of 10 different Jelly Belly jelly beans. The mean differences were determined. Each jelly bean flavor was provided to subjects prior to testing and subjects verified they had knowledge of what these flavors should taste like. Results: Significant differences($p<0.05$) were found between the means of: cappuccino 5.3, popcorn 5.2, mint chocolate chip ice cream 5.1, cinnamon 4.4, grape 4.2, mango chili 4.1, bubblegum 4.1, Tabasco 4.0, 7-UP 3.6, and cotton candy 2.9. Conclusions: Results confirmed in normosmic children Mozell's finding that coffee had the greatest retronasal component and Bartoshuk's observation that cappuccino jelly beans are the best testing agent to assess retronasal smell

#P6 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Examining the Relationship Between Subjective Smell Loss Ratings and Olfactory Test Performance in Traumatic Brain Injury (TBI) Patients Pursuing Injury Litigation

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In this study, we investigated the relationship between smell loss ratings and olfactory test performance in 45 traumatic brain injury (TBI) patients. The objectives of the study were (1) to determine if the relationship between ratings and performance differed among olfactory tests, and (2) to determine if the relationship between ratings and performance was significantly altered in TBI patients involved in litigation. Each patient completed Olfactory Threshold and Odor Identification (ID) testing. Further, each patient rated their smell loss on a scale from 0 (no disability) to 100 (maximum disability). When examining all TBI patients, regardless of litigation status, regression analyses in each test showed a significant relationship between ratings and performance. As ratings increased (more disability), performance on both tests decreased. However, when accounting for litigation, we found differences between groups.

For patients not involved in litigation, we found significant relationships between odor ID and ratings ($p<.001$), and between threshold and ratings ($p=.01$). Conversely, for patients involved in litigation, we did not find significant relationships between odor ID and ratings ($p=.072$), or between threshold and ratings ($p=.224$). From these results, we can conclude that there is a relationship between ratings and test performance when litigation status is not considered. However, this relationship is weaker (not significant) for TBI patients involved in litigation and these patients are not as accurate in rating their olfactory deficits. Though further study is warranted, this finding might point to a problem with malingering in this specific patient population, and suggests a need for more comprehensive olfactory testing when assessing TBI patients. Acknowledgements: Supported by NIH grant R01AG04085 to CM.

#P7 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Prenatal Alcohol Exposure Impairs Olfactory Function in Humans

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Children with histories of prenatal alcohol exposure often suffer devastating consequences. Fetal alcohol syndrome (FAS) is diagnosed by key facial features, growth deficits and CNS anomalies. Children with histories of prenatal alcohol exposure (EA) who do not exhibit all of the features of FAS also often have behavioral and cognitive impairments, though characterizing the EA phenotype remains challenging. Many of the regions impacted by EA (orbitofrontal cortex, medial temporal lobe, limbic areas) are critically involved in processing olfactory information, thus olfactory measures may contribute to better identification of EA. Although there are no publications reporting results of testing human olfactory performance in FAS or EA, studies of FAS in animal models suggest decreased olfactory bulb volume and the potential for impaired olfactory function. Here we compared children with EA to typically developing controls (NC) (N = 11/group). It was hypothesized that children in the EA group would perform more poorly than the NC group on the San Diego Odor Identification Test. The results showed that children with EA were significantly impaired in odor identification (M = 5.48, SE = .45) compared to typically developing age-matched controls (M = 7.16, SE = .45), $F(1, 19) = 6.83$, $p < .05$, partial $\square^2 = 0.26$. This is the first report of impaired odor identification in humans with EA. The results support compromised olfactory performance in EA, and suggest that further research is warranted to identify the mechanisms underlying these deficits, the integrity of brain areas that are involved, and to determine whether olfactory performance can contribute to better identification of children at risk for behavioral and cognitive deficits. Acknowledgements: Supported by NIH grants R01AG004085-25 to CM and R01AA010417-14 to EPR.

#P8 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Differences in Salivary pH and General Health Status Among Individuals Who Were and Were Not Breast-fed

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Past research shows positive effects of breast-feeding during infancy. The present study investigated adult salivary pH, adrenal level, and cortisol level, as well as general health indices, of 107 participants who were either breast-fed or not breast-fed as an infant. Data were subjected to independent t-tests, with group (breast-fed vs. non-breast-fed) serving as the independent measure and physiological measurements (salivary pH, adrenal level, and cortisol level) and general health indices serving as dependent measures. A significant pH difference was found between groups, with breast-fed individuals having more acidic saliva, $t(106)=-2.24$, $p=.03$. Differences between groups were also found for measures of health-consciousness [$t(64)=-1.78$, $p=.08$], health-status [$t(64)=2.01$, $p=.05$], healthiness-prevention [$t(64)=-1.65$, $p=.10$], and health-depression [$t(64)=-1.79$, $p=.08$]. Individuals that were breast-fed showed higher health consciousness, higher health status, higher health prevention, and lower health depression than non-breast-fed individuals. Implications of these results may influence mothers to consider their child's future general health in adulthood when deciding to breast-feed or use formula milk.

#P9 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Alliaceous Migraines

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Objective: To report a migraineur with osmophobia and trigger to garlic and onion Methods: 32-year-old woman; five years ago felt nasal pruritis upon eating red onion dip. Shortly thereafter, mere aroma of raw onions caused the sensation of her throat closing and panic attack. Over time, she developed headaches upon exposure to onions and garlic; preceded by aura of fortification spectra and visual entopia. Followed by a bipareital, crushing level 10/10 headache, burning eyes and nose, lacrimation, perioral paresthesias, generalized pruritis, nausea, fatigue, sore throat, dysarthria, confusion, dyspnea, palpitations, presyncopal sensations, hand spasms, tongue soreness, neck pain, phonophobia, and photopobia. These would persist for one hour after leaving the aroma. She is unresponsive to medication and wears a surgical mask when out. She also has chemosensory complaints: dysosmias every few months; phantosmias of food or cleaning products every month for a minute of level 5/10 intensity; palinosmia of onion or garlic odor for 30 minutes after exposure; metallic palinageusia after eating with metal utensils for a few minutes. Results: Neuro exam normal except for bilateral positive Hoffman reflexes. Chemosensory testing: QSIT 3/3, BSIT 12/12. MRI and CT with and without contrast

normal. Allergy skin test was positive for garlic and onion. Nose plug and counter stimulation with peppermint prevented the onset of migraine. Conclusion: This is the first report of migraines triggered by more than one alliaceous compound in the same individual. Possible mechanisms include odor induced: emotional change; vasomotor instability; trigeminal induced neurogenic inflammation; and allergic response. In alliaceous and odor-induced migraines, a trial of counter stimulation and nose plugs is warranted.

#P10 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Dysautonomia and Chemosensory Dysfunction

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Introduction: Myriad disorders associated with dysautonomias also display chemosensory dysfunction. Given this overlap, assessments of autonomic dysfunction amongst patients of a specialized chemosensory clinic were performed. Methods: 25 consecutive patients at a chemosensory clinic were approached to participate in this IRB approved study. 22 consented. Average age 51 years (range 22 - 69) 8 males and 14 females, with diagnosis of hyposmia/ anosmia (18), dysosmis (3), phantosmia (6), palinosmia (4), hypogeusia/ ageusia (15), dysgeusia (9), phantogeusia (9), burning mouth syndrome (4). All underwent the Quick Smell Identification Test (QSIT), and the Survey of Autonomic Symptoms (SAS) for symptoms and Total Impact Score (TIS) for severity. Results: Our patients demonstrated fewer autonomic symptoms than either those with autonomic disorders or even published controls. There was a significant difference in SAS score in the group as a whole (1.82) compared to published control SAS of $\leq$3.0 ($p= 0.003$) and of the group as a whole (4.32) compared to TIS of controls ≤ 7.0 ($p< 0.006$). No significance difference between QSIT score and either SAS or TIS was observed ($p>0.1$). Discussion: This lack of autonomic dysfunction in those chemosensory disorders may reflect a sampling error. Those with autonomic dysfunction may be so burdened by their primary illness they did not seek care for their chemosensory problems, if they even recognized them at all. Alternatively, the SAS and TIS may not be valid in this patient group, while physiologic autonomic testing might demonstrate dysfunction. A larger sample size may have revealed dysautonomia. Conclusion: Lack of autonomic symptoms were seen in those with chemosensory dysfunction. Further investigation of such a connection is warranted.

#P11 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

The WUTC Odor Threshold Test: Evaluating Olfactory Ability Using Signal Detection Theory

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A new odor detection threshold test (WUTC) was developed, using signal detection theory, to address the need for establishing a measure of consistency of subjects' responses, and the need for introducing different odorants to address different clinical/ research questions. The method of administration used is an improvement over previous methods of testing because the likelihood of desensitization to a single odor over time is minimized. Odorants were chosen on the basis of the possible link of the detection of specific odorants to known disease state. For example, using random presentation, 5 different odors were presented at 9 different levels of concentration twice to a subject with End Stage Renal Disease (ESRD). Blanks were presented 9 times also. Total administration time was 38 minutes. The subject was 100% consistent for isoamyl acetate, 89% percent consistent for P-cresol, and 44% consistent for vanillin and blanks, i.e. the consistency was less than chance suggesting that the subject was guessing. This result is consistent with the prediction that P-cresol may block the detection of vanillin in ESRD patients.
Acknowledgements: William H Wheeler Foundation

#P12 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Compensation Gone Awry: Conditions Inducing Regional Oral Sensory Loss May Elevate Obesity Risk

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Oral afferent nerves innervate portions of the mouth, convey unique arrays of information, and take different paths to the brain. As such, certain health conditions predict specific patterns of regional oral sensory loss: Severe childhood ear infections (otitis media, OM) damage the chorda tympani (CT) and block anterior taste cues, while tonsillectomy damages the glossopharyngeal nerve (IX) and blocks posterior taste/tactile cues. These local effects disinhibit intact oral sensations; for example, CT block elevates IX, trigeminal, and whole-mouth intensity, particularly in supertasters of 6-*n*-propylthiouracil. Although this compensatory mechanism often mitigates real-world (i.e., whole-mouth) perceptual deficits, our recent data implicate it in a more subtle trend toward long-term obesity risk. In a laboratory study ($N = 301$), individuals with medical histories indicating either CT damage (i.e., OM) or IX damage (i.e., tonsillectomy) show elevated whole-mouth taste, oral burn and viscosity, and retronasal olfaction (RO). In survey data from a larger sample ($N = 6584$), such individuals also

show increased high-fat food avidity and body mass. Consistent with reports linking RO to oral sensation, those with both OM and tonsillectomy show reduced whole-mouth taste and RO, revealing compensatory limits following extensive loss. While this model remains exploratory – it requires verification in a single sample, and shifts in obesity risk with whole-mouth gain vs. loss remain to be seen – relative intensity changes among flavor components appear sufficiently robust to influence high-fat intake. Overall, oral disinhibition sustains whole-mouth taste and flavor perception by moderating the impact of limited spatial loss, but the strength of this effect may shape long-term food choice and dietary health. Acknowledgements: NIDCD (DC 00283)

#P13 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Head Trauma, Taste Damage and Weight Gain

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Severe brain injuries associated with weight gain have been reported in children (Jourdan et al. 2012; Norwood et al. 2010) and adults (Henson et al. 1993); one source of the weight gain is believed to be metabolic (e.g., hypothalamic dysfunction). Head trauma has long been known to affect taste (Sumner 1967; Costanzo and Zasler 1991; Solomon et al. 1991). Our recent data suggest that taste damage from otitis media or tonsillectomy is associated with enhanced palatability of energy dense foods and weight gain (see Snyder & Bartoshuk poster). We presented a model suggesting that damage to taste nerves VII or IX could intensify non-taste oral sensations centrally possibly altering palatability (Bartoshuk et al. 2012). Of special interest, the consequences of damage to either VII or IX depended on the status of the other nerve. Central intensifications only occurred when the damage was restricted to one nerve. The present study extends these conclusions to taste damage resulting from head trauma. Subjects were healthy academics who reported they had experienced a concussion, loss of consciousness or loss of memory from a head injury. In a questionnaire study (N=3807), weight was significantly elevated and so was preference for high fat foods controlling for age and sex. Spatial taste testing (N=287) revealed significant loss of taste at VII with intensifications in flavor and oral touch (e.g., fat) in those subjects with intact IX. A third population is of special interest: athletes in contact sports like boxing or football who tend to gain weight in retirement. We suggest that food preferences should be examined in head trauma to determine how much weight gain can be attributed to taste damage with resulting sensory and palatability alterations. Acknowledgements: DC283, DC8613 and DC8620

#P14 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Atherosclerosis and Decline in Odor Identification

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Olfactory impairment is common in older adults although awareness of impairment is low, suggesting that olfactory function may decline slowly over time. We evaluated factors associated with a 5-year decline in odor identification in the Beaver Dam Offspring Study, a longitudinal cohort study of adults aged 21-84 years at baseline (BOSS1; 2005-2008). The 8-odorant San Diego Odor Identification Test (SDOIT) was administered at the baseline and 5-year follow-up (BOSS2; 2010-2013) examinations. Decline in odor identification was defined as a decrease in SDOIT score ≥2 from BOSS1 to BOSS2; no change was defined as a difference between BOSS1 and BOSS2 scores of ≤1. In preliminary analyses of the first 2195 participants with SDOIT data at BOSS1 and BOSS2, 3.1% had a decline in SDOIT score. Those with a decline in odor identification were more likely to be older (Odds Ratio (OR)=1.58, 95% Confidence Interval(CI)=1.40, 1.79, per 5 years of age) than those with no change in score. In age- and sex-adjusted models, baseline current smoking (OR=2.18, 95%CI=1.08, 4.37, vs never), carotid artery intima media thickness(IMT)(OR=1.17, 95%CI=1.01, 1.36, per 0.1mm), number of carotid artery sites (range 0-6) with plaque (OR=1.39, 95% CI=1.13, 1.70) and report of a head injury between BOSS1 and BOSS2 (OR=3.07, 95%CI=1.23, 7.64) were associated with an increased risk for decline in SDOIT score. In a multivariable model adjusting for age, sex and head injury, the number of carotid artery sites with plaque was an independent predictor of decline in SDOIT score (OR=1.37, 95%CI=1.11, 1.68). Smoking and IMT were not significant in models including plaque. These preliminary findings suggest atherosclerosis may be a contributor to, or marker of, the decline in olfactory function seen with aging. Acknowledgements: The project described was supported by R01AG021917 from the National Institute on Aging, National Eye Institute, and National Institute on Deafness and Other Communication Disorders. The content is solely the responsibility of the authors and does not necessarily reflect the official views of the National Institute on Aging or the National Institutes of Health.

#P15 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Measures of smell function in youth with autism

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Autism spectrum disorders (ASD) are pervasive developmental disorders characterized by deficits in social, communicative, and emotional behaviors. In addition to these hallmarks, there is evidence for atypical sensory processing. In particular, there is the suggestion of atypicalities in chemosensation, tested with either questionnaires or direct smell tests. Here we used both measures concomitantly. Sixteen youth with ASD (mean 15.3 yrs, 4 girls) and 16 typically developing youth (mean 14.3 yrs, 7 girls) participated. Self-reported sensory processing was measured with the Adolescent/Adult Sensory Profile. This 60-item questionnaire includes items related to the five major senses and conceptually arranged into four categories – "low registration" (i.e. low sensitivity to stimuli), "sensory sensitivity" (i.e. high sensitivity to stimuli), "sensation seeking", and "sensation avoiding". Smell function was measured with the pediatric Smell Wheel (Cameron & Doty, 2012). This scratch and sniff test measures the ability to identify 11 common odors using a 4-alternative forced-choice procedure using pictures and words to reduce cognitive load. Participants also rated the pleasantness of each odor. Youth with ASD scored significantly higher on "low registration", "sensory sensitivity" and "sensation avoidance", and significantly lower on "sensation seeking" ($p<0.05$). However the ASD and control groups did not differ in their ability to identify odors, nor were there differences in hedonic ratings of odors. More sensitive measures of olfactory function may be needed to detect differences in smell function in autism. Alternatively, self-reported sensitivity to olfactory stimuli may reflect altered perception of odors (e.g., heightened annoyance) rather than changes in sensory sensitivity.

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#P16 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Comparison of olfactory bulb neuronal phenotypes in control and Parkinson's Disease patients

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Olfactory dysfunction is found in nearly all sporadic cases of Parkinson's Disease and typically manifests years before motor symptoms are detected. Since the cellular mechanisms underlying this disruption of olfactory function are not understood, we have started immunohistological studies to establish whether select neuronal populations degenerate in the olfactory bulbs of Parkinson's patients. We are using olfactory bulbs from age- and sex-matched patients that were pathologically confirmed to be either control or Parkinson's Disease patients. These studies will examine the expression of tyrosine hydroxylase, calbindin and calretinin to assess whether subsets of inhibitory interneurons are altered. To address whether there are changes in the glutamatergic projection neurons, we will analyze the expression of Tbx21 since it is selectively expressed in the mitral/tufted cells. We will also address whether Parkinson's Disease disrupts either cholinergic or serotonergic centrifugal inputs to the olfactory bulb by analyzing the expression of choline acetyltransferase and serotonin, respectively. Together, these analyses will determine whether alterations in specific olfactory bulb neuronal populations underlie, at least partially, the cellular mechanism responsible for olfactory dysfunction associated with Parkinson's Disease, which will significant advance our understanding how the disease progresses and potentially provide insight for future studies to develop novel therapeutic strategies.

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#P17 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Waist to hip ratios predict odor recognition memory processing speed in carriers of the Apolipoprotein E ε4 allele

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The ε4 allele of Apolipoprotein E (ApoE ε4) is currently the strongest genetic risk factor associated with Alzheimer's disease (AD). Studies have linked the ε4 allele with olfactory decline. Previous research has also found that waist to hip ratios predict olfactory event-related potential (OERP) latencies among ε4+ individuals at the P3 cognitive component. The current study aimed to measure OERPs among ε4+ and ε4- individuals as they completed an odor recognition memory task and to determine whether the waist to hip ratio can predict the latency of the N1 sensory component of the OERP waveform. OERPs were recorded from the FZ, CZ, and PZ midline scalp electrode sites in 60 participants (30 F, 30 M, mean= 46.88 years) with an equal number of ε4+ and ε4- individuals. The odors were presented by a computer-controlled olfactometer. Participants were instructed that they were performing a memory task and completed three sessions: session 1 was an exposure trial for encoding, session 2 was a retrieval trial using odors, and session 3 was a retrieval trial using odor labels. Using a bivariate correlation analysis, results indicated a significant positive correlation between waist to hip ratio and N1 latency during odor retrieval hits for the FZ, CZ, and PZ electrode sites ($r = .358$, $p = .006$; $r = .352$, $p = .007$; $r = .334$, $p = .010$). When ApoE ε4 allele status was examined separately, the positive correlation remained significant for ε4+ individuals ($r = .439$, $p = .015$; $r = .423$, $p = .020$; $r = .425$, $p = .019$) but not for ε4- individuals. The results

suggest that latency of the N1 OERP component during retrieval of an odor recognition memory task may be a useful measure for examining the negative effects of high waist to hip ratios in those genetically at risk for AD. Acknowledgements: Supported by NIH grant # DC002064-14 from the NIDCD and A6004085-25 from the NIA. We thank Paul Gilbert for his statistical expertise and Derek Snyder, Jessica Bartholow, Roberto Zamora, Ariana Stickel, Kyle Sigel, Jean-Loup Bitterlin, Kristina Constant, and Sanae Okuzawa for helping with data collection, entry and analysis.

#P18 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Adverse effect of non-occupational atmospheric exposure to manganese on peripheral and central olfactory function

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Manganese (Mn), although an essential trace element, is of growing concern as a toxic air pollutant. It is not only readily transported from the olfactory epithelium (OE) to the olfactory bulb but, unlike other metals, is also transported transsynaptically to structures deep within the brain. However, to our knowledge no information is available on the possible effect of non-occupational exposure to Mn on olfactory function. We therefore investigated peripheral and central olfactory performance in a non-occupationally Mn-exposed population. Using the Sniffin' sticks test battery, we compared the olfactory performance of two groups (n = 30/group) from a Mn mining district in central Mexico: an exposed group living <1 km from a Mn processing plant, and a non-exposed control group living 50 kilometers from the closest source of exposure. Groups were matched for age, sex and schooling, and none had ever worked in mining-related activities. Concentrations of Mn in hair (MnH) were measured as a biomarker of exposure. Exposed subjects had significantly higher median MnH values (9.45 µg/g) than non-exposed subjects (1.04 µg/g). Furthermore, they were significantly out-performed by the controls on all olfactory measures (threshold, discrimination, and identification), indicating adverse effects of Mn exposure on a range of olfactory functions, including those involving higher-order cognitive processes. These results are in contrast to previous findings from our group showing adverse peripheral but not central effects on olfactory function of big city air pollution, which mostly consists of toxicants known to affect the OE but with lower transsynaptic transport capacity compared to Mn. Conclusion: non-occupational exposure to air-born Mn can adversely affect both peripheral and central olfactory function. Acknowledgements: MG received a doctoral grant from CONACYT.

#P19 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Odor perception and cerebral odor processing in adults with autism spectrum condition.

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Children and also adults with autism spectrum condition (ASC) are known to exhibit certain abnormalities in their sensory perception. However, there are only few studies on the sense of smell in autism. The aim of this study was to investigate whether there are differences in brain activation in response to odors between adults with autism spectrum condition and healthy controls. To this end both structural (volume of the olfactory bulb) and functional measurements (fMRI) were performed. In addition subjects underwent extensive psychophysical tests of olfactory function („Sniffin' Sticks": olfactory detection thresholds, odor identification). Twenty-two adults with ASC (high functioning autism and Asperger's syndrome) and 22 healthy controls were examined. Results indicate a significantly impaired olfactory threshold in ASC patients. In addition, olfactory identification was found to be significantly worse in patients with ASC. In terms of the size of the olfactory bulb no significant difference between the two groups was found. With regard to fMRI, ASC patients exhibited a higher level of overall activation in contrast to control participants. Furthermore, patients with ASC also showed significantly more activation in areas of the brain typically associated with odor processing, e.g. the orbitofrontal cortex and the limbic system. To summarize, even though impaired thresholds and results for odor identification indicate a lower level of olfactory function, a higher level of brain activation during odor processing was found.

#P20 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Subjective and objective olfactory abnormities in Crohn`s disease

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The pathogenesis of Crohn`s disease (CD) is still unknown. An involvement of the olfactory system in CD appears possible due to immunregulatory and environmental aspects. To date no study has systematically assessed the olfactory function in CD patients. Therefore, we investigated subjective and

objective olfactory function in CD patients. 31 CD patients in active disease, 27 CD patients in inactive disease and a control sample of 35 age and sex matched healthy volunteers were included in the study. Subjective testing was applied using the Sniffin Sticks Test. For olfactory testing olfactory event-related potentials (OERPs) were obtained by a four channel olfactometer using phenyl ethyl alcohol (PEA) and hydrogen sulfide (H_2S). Chemosomatosensory event-related potentials (CSSERPs) were obtained using carbon dioxid (CO_2) as a control stimulus. The analysis of variance revealed significant higher hedonic ratings for pleasant odorants in CD patients compared to healthy controls. Furthermore a trend to a lower threshold in CD patients in inactive disease occurred. In the objective olfactory testing CD patients showed lower base-to peak-amplitudes (N1) and lower peak-to-peak-amplitudes (P1-N1). Additionally the OERPs showed significant shorter N1- and P2-latencies following the unpleasant odorant (H_2S) in the right nostril for inactive disease compared to healthy controls. Our results demonstrate specific abnormities of olfactory perception in CD patients, which could be interpreted as a natural regulation against malnutrition. This points out the significance of the interaction between gastrointestinal functions and olfactory perception. Acknowledgements: ELAN-Application / FAU, in part by Neurotrition Project, FAU Emerging Fields Initiative.

#P21 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Effects of Parkinson's Disease on the Global Field Power of Olfactory Event-Related Potentials

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Aim: Measurement of event-related brain potentials in response to olfactory stimulation (OERPs) most often involves the amplitude and/or latency of specific components. These components however can be difficult to discern in OERPs from a single individual, especially one who is hyposmic. To circumvent this problem, we explored the use of an alternative measure that reflects the overall strength of an OERP: Its Global Field Power (GFP). Methods: The subjects were 20 patients with early-stage Parkinson's disease (PD) and 20 matched healthy controls. Stimuli consisted of 200 msec. presentations of hydrogen sulfide delivered via a continuous-flow olfactometer. OERPs were recorded at 40 electrode sites across the scalp and combined to form a single GFP trace based on their standard deviation at each time-point. Results: It was possible to obtain GFP measures for almost all subjects. The magnitude of change in GFP following odorant presentation, i.e. the overall strength of the OERP response, was smaller for PD than control subjects. Conclusions: While previous work has found effects of PD on OERP latency, the present study shows that there is an effect also on amplitude. More generally, this study demonstrates that a fully objective OERP measure is sensitive to olfactory function and can be obtained readily from single individuals. As such, OERP GFP may be of use in the clinic and well suited for standard statistical analyses. Acknowledgements: Supported by USAMRAA W81XWH-09-1-0467.

#P22 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Sensory Modality Influences Episodic Metamemory Accuracy in Healthy Aging and Alzheimer's Disease

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Episodic memory is commonly known to decline in both healthy aging and Alzheimer's disease (AD), however, these declines are heterogeneous. One factor shown to influence declines in episodic memory is metamemory, which is known to play an essential role in the strategies used for the encoding and retrieval of information, as well as the control of memory output (Pannu & Kaszniak, 2005). Prior research has shown that memory-based olfactory tests are useful in gauging cognitive decline in aging and AD (Murphy, Nordin, & Jinich, 1999), and the current study aimed to examine the utility of these tests in assessing declines in metamemory accuracy. Using a sample of 109 older adults with mild to moderate Alzheimer's disease and 97 healthy controls, the effect of diagnosis and sensory modality on metamemory accuracy (operationally defined as confidence in the accuracy of responses at retrieval) was analyzed using an episodic recognition memory task comprised of both olfactory and visual stimuli. Results indicated that both diagnosis and modality had main effects on confidence accuracy ($p < .05$). Overall, healthy older adults reported more accurate confidence levels than those with AD, and confidence levels for the odor modality were less accurate than for the visual modalities. Additionally, the interaction between diagnosis and sensory modality was significant ($p < 05$); controls reported significantly more accurate confidence levels in correct responses than those with AD in the visual modalities, but not the olfactory modality, indicating healthy older adults are no better at judging odor memory performance than those with AD, despite marked AD-related declines in olfaction. Applications and implications will be discussed. Acknowledgements: Supported by NIH grant # AG04085-25 (C. Murphy) with a Diversity Supplement (J. Szajer), and grant #AG005131-28 to the UCSD ADRC from the National Institute on Aging.

#P23 POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY

Primary Olfactory Cortex is affected in Alzheimer's Disease and Mild Cognitively Impaired Patients: A neuroimaging study

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Alzheimer's Disease is a neurodegenerative disorder affecting 5.4 million Americans and it is the 6th leading cause of death. Diagnosis of the disease is made when the pathology has progressed to the neocortex and the effectiveness of drug intervention is unlikely. Therefore, early diagnosis is key in understanding the disease progression and unlocking a cure. It has been shown that the pathology of AD (amyloid beta plaques (Aβ) and neurofibrillary tangles (NFT)) are first found in areas involved in olfaction. Decreased sense of smell is seen in the earliest stages of AD and in Mild Cognitive Impaired (MCI) patients. In this study we used olfactory functional Magnetic Resonance Imaging (fMRI) and volumetric MRI to examine the relationship between the functional deficit and the pathological changes (atrophy) in the primary olfactory cortex (POC) and in the hippocampus in 23 cognitively normal controls (NC), 19 MCI, and 15 AD subjects. The volumetric data shows that the volume of the POC is significantly different between the three groups (p <0.05); specifically the NC had a larger POC than the AD group. The fMRI data (p <0.05) also shows significant differences between the three groups (p <0.05); specifically the NC have significantly more activated voxels in the POC than the AD group. The volume and activation in the hippocampus were also measured to see how the POC compared. The volume of the hippocampus and POC are positively correlated as well as the number of activated voxels within the two regions of interest. These data show that the POC is involved in early AD and contributes to the olfactory deficits observed in early AD patients. Acknowledgements: Leader Family Foundation, NIH

#P24 POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY

The Effect of Abeta Accumulation on Odor Processing in Anterior Piriform Cortex

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Alzheimer's disease (AD) is a neurodegenerative disorder that is the main cause of dementia in the elderly today. Previous studies have implicated the accumulation of amyloid beta (Ab) in the brain as the hallmark pathology seen in AD. Patients suffering from AD often report problems with their sense of smell and indeed, cortical areas of the olfactory system are sites of early Ab deposition. Despite this temporal prominence, olfactory degeneration in AD remains under-explored. Here, we conducted a cross-sectional study using single-unit, ensemble and local field potential (LFP) recordings to assess odor-evoked responses in the anterior piriform cortex of anesthetized Tg2576 transgenic mice at 3, 6 and 12 months of age in order to investigate the effects of Ab accumulation on odor processing. Stimuli included both monomolecular odorants and complex odor mixtures. The mixtures allow assessment of pattern completion processing and are treated similarly in mice (shown here) as in rats (Barnes et al., Nat. Neurosci. 2008). Results suggest that, as previously reported, Tg2576 were impaired in an odor habituation task as compared to age-matched wild-type animals, Wesson et al. (J. Neurosci. 2010) and showed elevated aPCX LFP oscillations (Wesson et al., J. Neurosci. 2011).. Preliminary single-unit and ensemble results suggest enhanced spontaneous firing rates, abnormal odor receptive fields and impaired cortical ensemble decorrelation of overlapping odor mixtures in older Tg2576 mice compared to wildtypes. Ongoing analysis includes investigation of the age of onset of these single-unit, ensemble and LFP changes and how they correlate with Ab deposition in olfactory structures and the emergence of behavioral olfactory deficits. Acknowledgements: AG037693

#P25 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Differences in Odor Identification between Alzheimer's and Parkinson's Patients

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Whereas odor detection threshold is more impaired in patients with Parkinson's disease (PD) than Alzheimer's disease (AD), odor identification appears more impaired in AD than PD (Rahayel et al.'12). Failure to identify sensory stimuli can be induced by a sensory deficit (anosmia, failure to detect), a perceptual recognition deficit (apperceptive agnosia, ability to detect the odor without the ability to correctly describe the odor, and denies correct identification), or a failure of percept to access lexical semantic networks (anomia, inability to name with preserved ability to correctly describe the odor, select the name from choices or agree when told the correct name). The purpose of this study was to better understand the type of olfactory identification error exhibited in 22 participants with AD, 23 with PD and 45 matched controls (HC) during an open-choice olfactory task (NO) with 23 food items. The percentages of correct odor identification of AD (39%) and PD (42%) participants were not different, but both were significantly lower than HC (83%, $p<0.0001$). In contrast, the average NO intensity ratings of AD (29.3) were no different from HC (29.1) while PD average NO intensity ratings (14.5) were significantly lower than HC ($p=0.001$) and AD ($p=0.005$). In addition, the average percentage of anosmic NO responses was significantly higher in PD (41%) than in AD (21%, $p=0.001$) and HC (8%, $p<0.0001$). The average percentage of agnosic NO errors was significantly higher in AD (27%) than PD (8%) or HC (5%) ($p<0.0001$). Odor anomia was also significantly worse in AD (15%) than PD (8%) and both were significantly worse than HC (3%). While both PD and AD patients were impaired at NO identification, those with PD were more often ansomic and those with AD were more likely to have an odor agnosia and anomia.

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#P26 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Olfactory modulation of speech perception

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Speech perception can be modified by visual speech stimuli. The canonical example is the McGurk Effect in which discordant visual and auditory speech stimuli give rise to an illusory auditory percept that is different from the percept generated in the presence of concordant visual and auditory stimuli. Besides vision, tactile stimuli have also been shown to integrate with auditory speech, suggesting that shared information across modalities underlies sensory integration in speech perception. Here we investigate this by performing the McGurk paradigm in the presence of olfactory signals and examining the role of olfaction in modulating speech perception. Subjects watched video clips of a mouth articulating a word while they simultaneously inhaled a subthreshold pleasant or unpleasant smell, and indicated the word they hear. The connotation of the word can be positive or negative depending on the extent of visual-auditory integration. We find that olfaction is able to modulate the McGurk Effect, thereby showing the ubiquity of multisensory integration in speech perception.

#P27 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

The Dual Function of Basic Taste Stimuli: Signaling Nutrients in Smell and Taste

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Olfaction and taste are often considered important in guiding what we eat and drink. While much is studied about the involvement of taste in sensing nutrients, little is known about the role of olfaction in this process. Here we observe that the basic taste stimuli of monosodium glutamate (MSG) and sucrose, commonly thought to be odorless, generate distinctive olfactory sensations. In addition, subjects' olfactory sensitivity to MSG and sucrose, unlike that to a nonfood smell, is modulated by their physiological states of hunger and satiety. Furthermore, at suprathreshold, MSG and sucrose smells prolong the visual dominance of nutrient-congruent food in a binocular rivalry task; at subthreshold, MSG smell and taste summate and boost the visual perception of protein-rich food. These effects occur despite the fact that subjects are not verbally aware of the nature of the smells or their sensory differences. Our findings offer the tantalizing evidence that basic taste stimuli serve the dual function of signaling nutrients in smell and taste, and point to the hitherto unsuspected role of olfaction, alone or in combination with taste and vision, in monitoring homeostatic needs and guiding the search for nutrient-rich food.

#P28 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Taste and Odor Convergence in the Nucleus of the Solitary Tract of Awake, Behaving Rats.

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Although many studies have shown the importance of gustatory and olfactory interactions in flavor perception, very little is known about multisensory interaction in the initial stages of gustatory processing. Previously, it has been shown that a subset of cells in the nucleus of the solitary tract (NTS; Van Buskirk & Erickson, Brain Res.,135(2):287-303, 1977) and the parabrachial nucleus of the pons (PbN; Di Lorenzo & Garcia, Brain Res Bull.,15(6):673-6, 1985) in rats respond to both taste and olfactory stimuli. Here, we studied whether taste cells in the NTS of the awake, behaving animal could also respond to olfactory stimuli. Rats were surgically implanted with a microwire bundle into the NTS and allowed to recover. Rats were mildly water deprived and placed in an experimental chamber containing a lick spout for taste stimulus delivery and an odor port for olfactory stimulus delivery. Tastants (0.1 M NaCl, 0.1 M sucrose, 0.01 M citric acid, 0.0001 M quinine and artificial saliva) were delivered for 5 consecutive licks interspersed with 5 licks of artificial saliva rinse delivered on a variable ratio 5 schedule. All taste stimuli were presented both with and without an odorant in separate trials. Odorants were 1 Pa n-amyl acetate, 1 Pa acetic acid and air. Of the 31 cells recorded thus far, 74% were taste responsive, and 23% were odor responsive. There were no odor-responsive cells that were not also taste-responsive. When odorants are paired with taste stimuli, 96% of the 31 cells recorded showed either suppression or enhancement of taste responses. In addition, a small group of non-taste- or odorant-responsive cells (n = 8) responded when presented with a paired odorant-tastant stimulus. These results suggest that multisensory processing occurs at the initial stages of gustatory processing.
Acknowledgements: Supported by NIDCD grant RO1DC006914 to PMD.

#P29 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Enhancement of odor intensity and hedonics by taste: roles of nutritive taste and congruency

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We have previously shown that sucrose enhances the perceived intensities of congruent retronasal odors, whereas caffeine and citric acid do not. The present study is designed to investigate whether saltiness and umami can also enhance retronasal odors. In addition, given our previous finding that taste-odor congruency plays an important role in retronasal odor referral to the mouth, we tested the roles of congruency in the enhancement of odor intensities and hedonics. Tomato and chicken odors were presented alone or with NaCl, KCl, MSG, MPG, or caffeine. Using a sip-and-spit procedure, Ss rated 1) the degree of liking/disliking of flavor on the LHS; 2) the intensities of saltiness, savoriness, bitterness and specific odor on the gLMS; and 3) the degree of taste-odor congruency on a VAS. The result showed that both salty (NaCl) and umami (MSG, MPG) tastes significantly enhanced the perceived intensities of tomato and chicken odors (Tukey test, $p<.05$), while other tastes failed to enhance the odor intensities. Similarly, NaCl, MSG, and, to a lesser extent, MPG enhanced the degree of liking for both odors, whereas KCl and caffeine significantly decreased the odor liking ($p<.05$). The data also showed that the degrees of enhancement for both odor intensity and hedonics were significantly correlated with the degrees of taste-odor congruency ($r=.95$-$.99$, $p<.01$). Overall, our findings suggest that the presence of a nutritive taste (that signals the presence of a macronutrient) is required for retronasal odor enhancement to occur and that taste-odor congruency may further modulate the degree of odor enhancement. The current data also support the notions that salty and umami tastes can increase the palatability of food odors and that the degree of taste-odor congruency can predict the degree of flavor liking.

#P30 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

The primary qualities evoked by quinine, sucrose and capsaicin associate with propylthiouracil bitterness, but not TAS2R38 genotype

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Genetic variability in the ability to taste thiourea compounds has been studied for over 80 years. In the last 2 decades, the perceived intensity of concentrated propylthiouracil (PROP bitterness) has become a common measure of individual differences in taste response and taste acuity, as PROP associates with greater intensity responses from a broad range of stimuli, including non-bitter tastants, irritants and even retronasal aromas. However, early work indicated the putative receptor was specific for compounds containing the N-C=S moiety, and much but not all of the variation in PROP bitterness can be explained by polymorphisms in the TAS2R38 receptor gene. Still, it is hard to envision how a N-C=S specific receptor is related to overall orosensory response. Here, we report data for 100+ individuals tested in our laboratory who had been genotyped for TAS2R38 and phenotyped for PROP. These participants also reported the intensity of quinine, capsaicin, and sucrose on a general Labeled Magnitude Scale. Our data replicate earlier reports associating PROP bitterness with the primary qualities of sucrose, quinine and capsaicin. However, we also observed that the correlations between the intensity of sucrose, quinine and capsaicin were much stronger with each other than with PROP. As expected,

TAS2R38 genotype did not associate with the intensity of these sensations. When individuals were split by genotype, the strength of the PROP-capsaicin and PROP-sucrose relationships increased substantially within the groups of homozygous individuals. Collectively, this suggests PROP bitterness is a confounded phenotype that captures both genetic variation specific to N-C=S compounds and overall orosensory response. Acknowledgements: Supported by funds from the Pennsylvania State University and NIH grant DC0010904.

#P31 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

The Effect of Retronasal Odor on Ratings of Sweetness and Bitterness

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We report the first in a planned series of experiments on how odors affect rated bitterness, a potential flavor interaction that has received less attention than those with other taste sub-modalities (viz., sweet, sour, salty, and savory). These experiments used a computer-controlled olfactometer-gustometer to simultaneously present taste solutions and odorized air to the mouth. One experiment replicated a known effect, viz. enhancement of sweetness by a fruity-smelling ester, using the new olfactometer-gustometer. A second experiment examined the effect of a "burnt" odor on bitter intensity. Subjects included 12 healthy men and women, aged 18 to 65. Taste solutions included five concentrations each of sucrose (sweet) or sucrose octaacetate (SOA, bitter). Odorants included four concentrations each of ethyl hexanoate (sweet, pineapple) or isovaleraldehyde (burnt meat). Subjects held solutions in the mouth for several seconds, and rated the strength of both taste and odor sensations before expectorating. Subjects rated intensity using the general labeled magnitude scale (gLMS). Ratings of sweetness and bitterness increased with the concentrations of sucrose and SOA, respectively. This expected dose-response relationship supported the validity of the ratings. Further, consistent with published results, ethyl hexanoate significantly enhanced the rated sweetness of sucrose solutions. Thus, the current method of automated testing proved sensitive to known enhancement effects. Finally, isovaleraldehyde significantly enhanced the bitterness of SOA solutions, demonstrating that odors can enhance bitter taste. In conclusion, the method performed well, and modulation of bitter taste by retronasal odors seems like a promising area for further investigation.

#P32 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Understanding Valence: the Neurobiology of Appetitive and Aversive Odor-Taste Learning in Rats

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Appetitive and aversive conditioning both exert effects on perceptual learning, but are qualitatively distinct; for example, they evoke activity in different brain regions. Here, we present an olfactory conditioning paradigm capable of evoking both forms of conditioning with minimal procedural differences, enabling conditioning effects to be directly compared using identical behavioral and physiological analyses. Male Long-Evans rats (*Rattus norvegicus*) served as subjects for this study. Using implanted intra-oral cannulae, appetitive or aversive tastants (0.20% saccharin or 0.02 *M* quinine) were directly infused into rats' mouths and paired (or backward-paired) with an odor conditioned stimulus over 3 days such that training procedures differed only in the valence of the tastant. Rats displayed appropriate anticipatory behaviors (rapid mouth movements, tongue protrusions, gaping) in response to odors predicting tastant infusions, indicating that rats learned the association between odors and tastants. Aversively-conditioned rats also appeared to exhibit broader generalization to similar odorants than did the appetitive and control groups. Immediate-early gene (Egr-1 and *c*-Fos) expression was measured in olfaction-, valence-, and conditioning-associated brain regions. IEG expression was higher in the main olfactory bulb, anterior olfactory nucleus, piriform cortex, and orbitofrontal cortex in aversively-conditioned rats compared with appetitive and control groups. These results provide a foundation for studies of learning and plasticity in which appetitive and aversive associations can be mechanistically compared in a common neural network. Acknowledgements: Liu Memorial Award, Sigma Xi Research Grant, Cornell University SAGE Fellowship

#P33 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Pou2f3/Skn-1a is involved in the differentiation of multiple types of Trpm5-expressing chemosensory cells

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A homeodomain transcription factor Pou2f3 (also known as Skn-1a) is specifically expressed in sweet, umami, and bitter taste receptor cells in taste buds, and is necessary for their functional differentiation[1]. Recent studies have shown that taste receptors and/or signaling molecules indispensable for sweet, umami,

and/or bitter taste are expressed not only in gustatory tissues but also in the intestinal and respiratory epithelia. In this study, we examined the expression of Pou2f3 in the extra-oral epithelial chemosensory cells and the impact of Pou2f3 knockout on the cells. In the intestinal epithelium, the expression of Pou2f3 was observed in the tuft/brush cells that express Plcb2 and Trpm5 and participate in opioid secretion by chemosensing. Pou2f3-deficient mice lacked the expression of Plcb2, Trpm5, and other tuft/brush cell marker genes, but they still expressed characteristric genes of enteroendocrine cells. In the respiratory epithelium of the nasal cavity, the expression of Pou2f3 was observed in the solitary chemosensory cells (SCCs) that express Tas1r3, Tas2rs, Gnat3, Plcb2, and Trpm5. The expression of all these genes was lost in the Pou2f3-defficient mice. We also found Pou2f3 expression in a subset of microvillus cells in the main olfactory epithelium (MOE) where Trpm5 but not Plcb2, Ggust, or taste receptors were expressed. Pou2f3-deficient mice exhibited the lack of Trpm5 expression in the MOE. Taken together, these data demonstrate that Pou2f3 expression is associated with the expression of Trpm5 in multiple types of chemosensory cells, and suggest that Pou2f3 is a master regulator of differentiation of Trpm5-expressing chemosensory cells in digestive and respiratory epithelia. [1]Nat. Neurosci. 14, 685-687 (2011)

#P34 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Aronia Berry Juice Sensory Analysis by Harvest Time and Oral Sensory Phenotype

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Aronia berries (chokeberries) have very high levels of health-promoting antioxidants yet can cause a "choking" sensation due to bitterness and astringency. We aimed to describe oral sensations and palatability of aronia juice, including variation by harvest time and oral sensory phenotype. Ripe aronia berries were harvested at 7 time points and juiced for oral sampling by 50 adults who were phenotyped for chemosensory function by the NHANES protocol, olfactometer, and propylthiouracil (PROP) bitterness. The adults reported quality intensities of prototypical tastes, oral chemesthetic compounds, foods, berry juice and non-oral stimuli, which served as sensory standards. The juice qualities correlated with alum astringency, quinine bitterness, and citric acid sourness but, unlike apple or grapefruit juices, did not correlate with sucrose sweetness. The average berry juice response was weakly dislike (range—v. strongly dislike to above moderately like). Astringency was the strongest sensation, yet sweetness was the primary driver of liking in multiple regression analysis. Those who liked the juice reported a greater balance between astringency and either sourness or sweetness. The juices were more sweet and less sour/astringent in the middle versus first harvest time, corresponding to greater acceptance. Classifying by PROP relative to quinine bitterness identified adults who differed in intensities of prototypical oral stimuli but not in intensities of odors. Those who perceived more PROP relative to quinine bitterness also reported the juice as less sour, less balanced between astringency and sourness, and more disliked than those who perceived high bitterness from PROP and quinine. Further study aims to identify ways to maximize the palatability of aronia juice, individualized to taste phenotype. Acknowledgements: USDA/Hatch and USDA NE SARE

#P35 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Temperature of served water can influence sensory perception and acceptance of subsequent food

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The cross-cultural difference in meal pattern exists in the typical temperature of water served with meals. For example, North American people, as a whole, are used to drinking iced water/beverages, while Asian or European people show a preference for hot water/tea or room temperature water, respectively. It has been proven that food perception and acceptance are affected by oral temperature, as well as by serving temperature of food. Based on the fact that the iced or hot water served with meals can modulate the oral temperature, the present study aimed to determine if the temperature of served water can modulate the sensory perception of foods subsequently consumed. Following a mouth rinse with water served at 4, 20, and 50 °C for 5 s, two types of food: dark chocolate or cheddar cheese were evaluated in terms of sensory intensity and overall liking. For the dark chocolate, the intensity ratings for sweetness, chocolate flavor, and creaminess were significantly lower when following water at 4 °C than when following water at either 20 or 50 °C. However, the effect of water temperature on sensory perception was not observed with cheddar cheese. In addition, the overall liking for the dark chocolate was significantly lower when following water at 4 °C than when following water at either 20 or 50 °C. In conclusion, the current study demonstrates new empirical evidence that the consumption of iced water can decrease perceived intensities of sweetness, chocolate flavor, and creaminess for subsequently consumed chocolate. Our findings suggest a possibility that the North American frequent consumption of iced water/soda may reduce their sensitivity to sweet tasting stimuli, thereby leading to the preference for more highly sweetened foods. Acknowledgements: This research was supported by start-up funding from the University of Arkansas Division of Agriculture to HS SEO.

#P36 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Stimulus temperature and concentration differentially influence the gustatory neural code for sucrose in the mouse brain stem

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Taste sensitive neurons throughout the gustatory neuraxis respond to oral somatosensory stimuli, like temperature. What is more, human psychophysical studies show that unimodal oral thermal stimuli can elicit taste perceptions, and increasing the temperature of a sucrose solution increases its perceived "sweetness". These data suggest that temperature may be modulating the neural signal for taste intensity. However, data on this topic are scarce. To investigate the potential influence of temperature on neural activity for taste intensity we made extracellular recordings from single neurons in the rostral nucleus of the solitary tract of anesthetized C57BL/6J mice during oral application of temperature-and concentration-varied tastants. Stimuli included purified water and a concentration series of sucrose (in M): 0.05, 0.1, 0.17, 0.31, and 0.56 presented "whole mouth" at 17, 22, 30, and 37° C. Preliminary analyses of 35 neurons show that warming sucrose to 37° C significantly reduced the response onset latency compared to room temperature sucrose for all concentrations tested (ps <0.01). Multivariate analysis shows that temperature can substantially change stimulus-evoked across-neuron patterns of response in a way that differs from the influence of concentration. These analyses suggest that temperature is modulating taste responses in a unique way compared to concentration, suggesting temperature may be a parameter of the taste code. Acknowledgements: NIH DC011579 (C.H.L.)

#P37 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Olfactory modulation of visual temporal processing

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Perception is thought to consist of fast 'snapshots' of the world on a need-to-know basis. We ask if additional information from the olfactory channel, which naturally conveys object identities, influence the temporal encodings in the visual system. Using a two-alternative forced choice method, we find that a smell lengthens the subjective duration of a sensory congruent visual object and enhances its visibility at frequencies near critical flicker fusion (CFF) in a manner independent of top-down cognitive control. In the latter case, the behavioral advantage is accompanied by increased power of neural oscillatory responses over the occipital-temporal region around the frequency of the flickering visual object. These results indicate that olfaction modulates visual temporal processing at the object representation level, and provide new insights into the neural timing of multisensory events. Acknowledgements: National Basic Research Program of China (2011CB711000), National Natural Science Foundation of China (31070906), National Natural Science Foundation of China (31100735), Knowledge Innovation Program of the Chinese Academy of Sciences (KSCX2-EW-BR-4 & KSCX2-YW-R-250)

#P38 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

The Ice-Cream Effect: The Influence of Temperature on Taste Perception

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The *Ice-cream Effect* is a term coined to describe the anecdotally reported difference in perceived taste intensity of a product at different temperatures e.g. when using fruit juice or syrup to make ice cubes, a more concentrated mix is ideal for optimum taste when frozen compared with the strength of a regular drink. The main objective of this study was to investigate how temperature influences perceived taste intensity and hedonic value for different solutions. 20 females and 10 males (aged 18-34 years) evaluated solutions of Sucrose (100g/L), Sucralose (0.254g/L), Na salt (8g/L), Na/K salt mix (1:2 ratio, 11.128g/L) and milliQ water at approximately 1 (cold), 22 (ambient) and 50°C (hot) using a *sip and spit* method. Solutions were presented as 10mL samples in randomised order and in duplicate. Participants rated the perceived intensity of four basic tastes (Sweet, Salt, Bitter, Sour), temperature and pleasantness on 10cm VAS for each sample. Overall there was no significant effect of temperature on perceived taste intensity. Hot milliQ samples were rated sweeter than ambient samples (p=0.038) and hot Na/K salt samples as more pleasant than ambient or cold (p=0.024). Gender effects were found for perceived sweetness of Sucrose (Females rated > Males, p=0.016) and pleasantness ratings of Na and Na/K salt samples (Males rated > Females, p=0.017 and 0.001). Gender*Temperature interaction was found for pleasantness of Na/K salt samples (p=0.025). Contrary to expectations, temperature did not have a significant effect on perceived taste intensity. Nevertheless, it is suggested that sweet and salt tastes have greater hedonic value at temperatures other than ambient and that factors such as changes in texture and oral exposure time should also be considered as the basis for the 'Ice cream effect'.

#P39 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Evidence for a Cell Fate Refinement Mechanism in Olfactory Sensory Neurons

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Olfactory receptors (ORs) number more than 1,000 and comprise the largest gene family in the mammalian genome. ORs reside in heterochromatin and selection of one OR and from one allele is thought to occur stochastically. ORs are expressed both monogenically and monoallelically in olfactory sensory neurons (OSNs) and the mechanism that controls their regulation is largely unknown. Here we describe results for mice with a 'monoclonal' nose that express one OR M71in 95% of all mature OSNs. M71 mice suppress expression of endogenous ORs, and expression of the suppressed ORs is shifted to the immature layer of the olfactory epithelium. We show that the suppressed ORs were first selected and then turned off by M71. When we introduced a second transgene into M71 mice that expressed another OR in most mature OSNs, OSNs uncharacteristically expressed both of the ORs. We hypothesize that unresolved OR competition compromised the neuron's ability to express only one receptor. We further show that suppression of endogenous ORs by M71 is not reversible, and that M71 does not need to be continuously expressed for endogenous ORs to remain suppressed. In these experiments, we have engineered OSNs to express more than one OR in an OSN at a time, which is normally a low probability event. We have shown that when this event arises, a secondary refinement pathway is invoked that turns off one OR to maintain singular expression. We thus provide compelling evidence for a new paradigm of OR regulation: *post-selection shut down*, which we hypothesize occurs through a yet-to-be uncovered competitive mechanism.

#P40 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Odorant Receptor Dependent Spontaneous Firing Rates Do Not Predict Sensory-evoked Firing Rates in Mouse Olfactory Sensory Neurons

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Sensory systems need to tease out stimulation-evoked activity against a background of spontaneous activity. In the olfactory system, the odor response profile of an olfactory sensory neuron (OSN) is dependent on the type of odorant receptor it expresses. OSNs also exhibit spontaneous activity, which plays a role in establishing proper synaptic connections and may also increase the sensitivity of the cells. However, where the spontaneous activity originates and whether it informs sensory-evoked activity remain unclear. We addressed these questions by examining patch-clamp recordings of genetically labeled mouse OSNs with the defined odorant receptor M71 (n = 22), I7 (n = 21), SR1 (n = 11), mOR-EG (n = 24) or MOR23 (n = 16) in intact olfactory epithelia. We show that OSNs expressing different odorant receptors had significantly different rates of basal activity. Additionally, OSNs expressing an inactive mutant I7 receptor completely lacked spontaneous activity (n = 34), despite being able to fire action potentials in response to current injection (n = 6). This finding strongly suggests that the spontaneous firing of an OSN originates from the spontaneous activation of its G-protein coupled odorant receptor. Lastly, we show that the spontaneous firing rates of selected OSN types do not correlate with the firing rates evoked by a near-saturating odorant stimulus. This study reveals that neither the basal activity nor the receptor type dictates the maximum odorant-evoked activity in OSNs, which suggests that OSNs expressing the same receptor type may send distinct information to the brain upon odorant stimulation. Acknowledgements: This work was supported by R01 grants from NIDCD/NIH (DC006213 and DC011554).

#P41 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

How plastic is the peripheral olfactory system of *Drosophila melanogaster* larvae?

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During their larval stage, fruit flies are exposed to an odour-rich environment, in which they must choose between toxic and edible substrates. For this they need an efficient olfactory system with the capacity for both short and long term plasticity. *Drosophila* larvae possess only 21 paired olfactory sensory neurons (OSN), most of which express a single olfactory receptor (OR) type together with the co-receptor Orco. Information arising from each OSN is transmitted to a unique glomerulus in the antennal lobe and then to the mushroom body via projection neurons. Combinatorial coding in the periphery allows larvae to detect and discriminate a large number of odours. Previous studies have characterised the odour-response profiles of 19 of the 21 OSNs and found that a given OSN's response to a given odour is often highly variable (Hoare et al 2008, 2011). This raised the possibility that the peripheral olfactory code exhibits plasticity and that this plasticity may be directly involved in mediating behavioural adaptation and learning. We are exploiting the UAS-Gal4 system to create single OR lines in which only one identified OSN is functioning. We are studying the effect of short and long-term adaptation on the response of individual OSN classes to a panel of odours using extracellular electrophysiology and behavioural assays. Our preliminary results show that short-term adaptation to specific odours may induce a decrease or an increase in OSN responses depending on the odour used. We are currently exploring the effect of longer-term adaptation on the peripheral olfactory code. Acknowledgements: BBSRC UK grant BB/H009914/1

#P42 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Characterization of the Iontransporter NKCC1 in the Field of Chemosensation

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The olfactory sense is mainly regulated through a cAMP-dependent signaling cascade which leads to a cation influx and a chloride efflux through the neuronal membrane. This so called chloride boost during depolarization of olfactory sensory neurons still remains unclear. In addition, how is the intracellular chloride concentration achieved in olfactory neurons? Several publications demonstrated that the chloride concentration is much higher in olfactory neurons, especially in the knob, compared to surrounding cells and the mucus. NKCC1 is a candidate which fits the role of an ion transporter that causes the high chloride concentration inside olfactory neurons. NKCC1 is a 12 membrane spanning symporter of one sodium, one potassium and two chloride ions. The expression of NKCC1 is confirmed in the olfactory epithelium of mice, especially in olfactory neurons. However, the function of NKCC1 is controversially discussed in literature. In our project we want to characterize NKCC1 knockout mice, thereby addressing the question whether NKCC1 is involved in olfaction and olfactory neurogenesis. On the one hand we are going to use chloride imaging of acute slices of the olfactory epithelium of knockout and wild type mice. On the other hand morphological studies and RNA fluorescence *in situ* hybridization (RNA FISH) experiments will give us information about the role of NKCC1 in neurogenesis. Our first studies showed differences in the morphology of the turbinates and the neuronal layer of the olfactory epithelium of NKCC1 knockout compared to wild type mice leading to the question whether NKCC1 plays a role in the continuous replacement of olfactory sensory neurons.

#P43 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Intrinsic electrophysiological property of Kenyon cells in silkmoths

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Kenyon cells (KCs) are the component neurons of mushroom bodies (MBs) of insect brain regions contributing to olfaction and taste. In these contributions, KCs may have some important roles in olfactory information processing. However, the intrinsic electrophysiological properties of silkmoth KCs remain unknown. Here, we use whole-cell patch clamp recording to elucidate the functional parameters such as voltage-activated ionic currents of KCs in silkmoth MBs. KCs generated action potentials in response to depolarizing current injections which were stepped in 20 pA between 0 and 100 pA, and application of GABA-receptor blocker, picrotoxin (PTX) abolished inhibitory synaptic inputs and depolarized resting potential. By using voltage-clamp technique, we recorded membrane currents including inward and outward voltage-activated currents. Pharmacological isolation of KC voltage-activated ionic currents revealed that KCs express a range of voltage-activated currents, including transient ($I_{transient}$; activated by voltage step pulses above -50 mV) and non-activating potassium ($I_{sustained}$; activated by voltage step pulses above -30 mV), sodium (I_{Na}; activated by voltage step pulses above -50 to -40 mV) and calcium (I_{Ca}; activated by voltage step pulse above -60 to -50 mV) currents, and these potassium currents included calcium-activated components. Our results consisted with previous research of cockroach (Demmer and Kloppenburg. 2009) and provided the first electrophysiological characterization of KCs in silkmoth MBs and suggested that the intrinsic properties of KCs had common feature regardless of the insect species. Our experiments represented an important step toward understanding neural computation that underlies olfactory information processing in silkmoth.

#P44 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Scaffolding proteins in olfaction

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Mammalian olfactory signaling is dependent on various proteins and fine-tuned through different processes. Most of the essential components are already known but the detailed organization of this complex system has yet to be understood. In our recent study we identified the multiple PDZ domain protein MUPP1 as a potential scaffolding protein candidate for olfactory signaling. Through large-scale peptide microarrays we could show numerous interactions between the 13 PDZ domains of MUPP1 and different murine olfactory receptor C-termini of various subfamilys. Co-immunoprecipitations validated the interactions between MUPP1 and the most important signaling proteins in vivo and led to the assumption that an olfactory PDZome is organized by the scaffold MUPP1. Furthermore co-immunoprecipitations in juvenile mice showed no differences in binding properties in comparison to the adult mice. To functionally show that olfactory signaling is PDZ-dependent we established patch clamping of olfactory sensory neurons in acute slices of transgenic mOR-EG mice. We also created a small inhibitory peptide which disrupts the interaction between

the mOR-EG receptor and MUPP1 and injected it through the patch pipette into the neuron. After uncoupling the interaction between the mOR-EG receptor and MUPP1 the odor-evoked current amplitudes were strongly reduced and the adaption was impaired, whereas a control peptide did not affect olfactory signaling. In conclusion, we confirmed that an olfactory signalosome is mediated by MUPP1 in olfactory sensory neurons and showed that accurate olfactory signaling is a PDZ dependent mechanism.

#P45 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Expression of olfactory signaling molecules in the non-chemosensory tissues

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Olfactory sense is mediated by specialized olfactory receptor neurons (ORNs) in the nose. However, ectopic expressions and functional roles of olfactory receptors (ORs) and olfactory signaling molecules (OMP, $G\alpha_{olf}$, and AC3) still remain to be elucidated. This study demonstrates the presence of olfactory signaling molecules in non-olfactory tissues by systematically using RT-PCR, western blotting, immunohistochemistry, and a double-antibody immunoprecipitation/immunodetection procedure. Unexpectedly, the co-localization of OMP/AC3/$G\alpha_{olf}$ was confirmed in several tissues while they were expressed on different cell types of the same organ in another non-chemosensory tissue. Additionally, gene expression of olfactory receptors (ORs) was observed in non-olfactory tissues through RT-PCR. These results suggest that olfactory receptors play an important role in tissue-specific or common physiological functions of ectopic expression in non-olfactory tissues. In the future, we need to define the physiological function of olfactory receptors in non-chemosensory tissues. Acknowledgements: DGIST MIREBrain and Convergence Science Center (13-BD-0403)

#P46 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

In vivo dynamic interactions between the methyl-CpG binding protein MeCP2 and chromatin under odor-evoked activity

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MeCP2 was identified as a methyl-CpG binding protein and capable of recruiting co-repressor complexes to promoters to suppress gene expression. MeCP2 is abundant in neurons. Mutations in *MECP2* cause Rett syndrome, a neurodevelopmental disorder. Recent studies suggest that *Mecp2* has multiple functions including transcriptional repression/activation and structural compaction of chromatin. Dynamic interaction between MeCP2 and chromatin is not well understood. The complexity of MeCP2 function among different neuronal populations and a different methylation status in *in vitro* culture system have made it challenging to understand MeCP2 binding profile and dynamics under neuronal activity *in vivo*. Olfactory epithelium provides an ideal *in vivo* model in its ubiquitous neuronal population and accessibility for neuronal activity manipulation. In this study, we sought to identify MeCP2 binding profiles to different regions of the chromosome and changes under odor-evoked activity. Chromatin immunoprecipitation following high throughput sequencing shows MeCP2 binds to not only methylated CpG island but also intergenic and intronic regions and sparsely methylated promoters. Genome-wide profiling for MeCP2 binding *in vivo* clearly shows two distinct distributions of MeCP2, one concentrated at regulatory regions and the other along the entire genes locus. Odor-evoked activity results in significant changes in MeCP2 affinity to selected gene loci. Comparing methylation state and MeCP2 binding profiles revealed that odor-evoked activity alters MeCP2 affinity to chromatin in a DNA methylation independent manner. Our results reveal the complexity of MeCP2 and chromatin interaction. We hypothesize that Mecp2 regulates activity-dependent gene regulations via changing its binding affinity to the entire gene locus. Acknowledgements: NIH DC11346

#P47 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Sensory inputs modulate olfactory cilia morphology and function in the mammalian nose

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By converting environmental signals into intracellular responses, cilia are critical for many biological processes, including olfaction. Surprisingly, little is known about what factors shape cilia morphology and how morphology impacts function. We recently discovered that olfactory cilia vary considerably in length depending on the cell location within the olfactory epithelium. Using specific markers for a subset of olfactory sensory neurons (OSNs) from C57BL/6 mice (3-6 weeks, n = 19 animals), we found that cilia length increases from ~1 μm in the posterior nasal septum to ~20 μm in the anterior septum, with the longest cilia (up to 50 μm) typically found in the dorsal recess. We then built a 3D computational fluid dynamics model based on the mouse nasal cavity and demonstrated that cilia length is positively correlated with sensory inputs, particularly odorant absorption. To determine whether sensory inputs themselves account for the cilia length pattern, we performed unilateral naris closure on newborn mice (n = 6 animals) and immunostained

olfactory cilia four weeks later. Remarkably, cilia length was increased in the open (overstimulated) nostril. We further found that cilia length modified OSN function, as OSNs expressing a defined odorant receptor were more sensitive to odorant stimulation when they had longer cilia (n = 7) as opposed to shorter cilia (n = 8). Together, these results suggest that sensory activity may shape olfactory cilia length and, consequently, OSN function. This discovery offers novel insight into the organization and function of OSNs and into cilia biology. Acknowledgements: Supported by NIDCD grants R01DC011554 and R01DC006213.

#P48 POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY

SUMOylation regulates the ciliary localization of olfactory signaling proteins

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In olfactory sensory neurons (OSNs), the protein components for odor detection are highly enriched in cilia, however the precise mechanisms for this localization remain poorly defined. The mechanisms for selective cilia entry may be analogous to nuclear import utilizing importin ß2, a Ran gradient and nucleoporins. A unique post-translational modification process involved in nuclear-cytosolic transport is the reversible conjugation of Small Ubiquitin-like Modifier (SUMO) proteins or SUMOylation. Bioinformatic examination reveals that both adenylate cyclase 3 (AC3) and the calcium-activated chloride channel, annoctamin2 (ANO2) harbor conserved SUMOylation motifs. Therefore, we hypothesized that SUMOylation regulates ciliary localization of AC3 and ANO2. Coexpression of SENP2, a SUMO protease, with either AC3:GFP or ANO2:GFP in MDCKII cells prevented their normal ciliary localization. Site directed mutagenesis of the predicted SUMOylation sites also blocked ciliary localization of both proteins. To test if SUMOylation is necessary for trafficking of signaling proteins *in vivo*, mice were dually infected with wildtype or mutant adenovirus constructs along with Arl13b:mCherry (a cilia marker). Live, *en face* imaging of OSNs showed wildtype AC3:GFP co-localized with Ar113b:mCherry in olfactory cilia, while the mutant form failed to enter olfactory cilia. Surprisingly however, both wildtype and mutant ANO2:GFP trafficked into olfactory cilia, indicating potential other mechanisms permitting trafficking *in vivo*. In addition, the generation of SUMOylation sites in the related channel, ANO1 was not sufficient for ciliary entry. Together our data demonstrate that SUMOylation of some signaling proteins is necessary, but not sufficient for ciliary localization. Acknowledgements: This work was supported by NIDCD grants 1R01DC009606-01 (JRM) and 1F32DC011990-01 (JCM)

#P49 POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY

Functional characterization of alternative signal transduction pathways in olfactory receptor neurons

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It is generally agreed that in olfactory sensory neurons (OSNs) the binding of odorant molecules to their specific olfactory receptor (OR) triggers a cAMP-dependent signaling cascade activating cyclic-nucleotide gated (CNG) channels. However, considerable controversy dating back more than 10 years has surrounded the question of whether phosphoinositide (PI) signaling plays a role in mammalian olfactory transduction. Early studies of PI signaling in olfaction focused solely on the classical phospholipase C (PLC) dependent pathway, demonstrating that odorants can elevate inositol triphosphate (IP3). In addition, our recent study proved that odorants stimulate both, PLC and phosphatidylinositol 3-kinases (PI3Ks) in the dendritic knobs and in olfactory cilia of rodent OSNs. In this project, we aim at characterizing the dual pathway of olfactory signaling in more detail. For this purpose, we will analyze the distribution of PI signaling upon specific odor stimulation in living OSNs via translocation imaging. The use of mOR-EG-GFP transgenic mice will allow for specific analysis of OSNs expressing the well-characterized olfactory receptor mOR-EG, which can be activated by different odorants. To investigate PI signaling in OSNs, we will use adenoviral vectors carrying two different fluorescently tagged proteins, the pleckstrin homology (PH) domains of phospholipase C (PLC) and the general receptor of phosphoinositides (GRP1), to monitor PI activity in the murine olfactory epithelium *in vivo*. Furthermore, we will monitor the effects of PI signaling on the electrophysiological output of OSNs by patch clamp technique of single neurons in acute OE slices of mOR-EG-GFP transgenic mice.

#P50 POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY

Phospholipase C Mediates Intracellular Ca^{2+} Increase via Internal Ca^{2+} Stores and trpM5 Activation in Mouse Olfactory Sensory Neurons

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Phospholipase C (PLC) and internal Ca^{2+} stores are involved in a variety of cellular signaling including sensory transduction. However, our understanding of the PLC pathway in mammalian olfactory sensory neurons (OSNs) is largely limited to those studies in which the PLC inhibitor U73122 was used to suppress

odor responses. Recently, transient receptor potential channel M5 (trpM5) has been shown to express in a population of mature OSNs in mice (Lin et al 2007). trpM5 is an essential downstream effector of the PLC pathway for taste transduction. Here we investigate PLC, trpM5 and internal Ca^{2+} stores in freshly isolated mouse OSNs using single cell Ca^{2+} imaging.
We found that OSNs responded to a PLC activator m-3M3FBS in a concentration dependent manner with a higher percentage of responding cells and greater amplitudes after an increase in concentration (78%, n=23 at 15μM, 90.3%, n=52 at 25μM). In contrast, only one out of 9 OSNs responded to the inactive analog o-3M3FBS (25μM). Eliminating extracellular Ca^{2+} did not reduce the percent of responding OSNs to m-3M3FBS and only the response amplitudes were moderately reduced (n=7). In addition, The PLC inhibitor U73122 (5-10μM) greatly reduced the percent of OSNs responding to m-3M3FBS (37.5%, n=8) and the response amplitudes. Further, using OSNs isolated from trpM5-GFP and trpM5 knockout-GFP mice, we found that trpM5-expressing OSNs responded to m-3M3FBS with a significantly larger amplitude and calcium load than the trpM5-null OSNs (n= 6 to 9 for each group). Our data suggest that most OSNs are capable of utilizing the PLC pathway to release Ca^{2+} from internal Ca^{2+} stores and that subsequent activation of trpM5 in trpM5-expressing OSNs leads to additional increases in intracellular Ca^{2+} loads. Acknowledgements: Supported by research grants NIH/NIDCD 009269, 012831 and ARRA administrative supplement to WL

#P51 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Analysis of the novel protein Q8BH53 in olfactory sensory neuron cilia

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The cilia of olfactory sensory neurons (OSNs) are specialized for encoding and transducing odor information. Among the proteins found in the cilia, many are critical for mediating and/or modulating olfactory signal transduction. We detected a novel protein, Q8BH53, from a proteomic screen of OSN cilial membrane preparations. Q8BH53 is conserved among eukaryotes and is a unique protein, as no other paralogs exist in the mouse genome. Bioinformatic analysis suggested that the majority of the Q8BH53 sequence is composed of ARM-domains. Although the function of Q8BH53 is unknown, the presence of these ARM-repeat domains signifies that it may be important for establishing protein-protein interactions. *q8bh53* transcripts are abundant in the mouse olfactory epithelium and are also found in several other tissues. Using immunohistochemistry, we found that Q8BH53 localizes specifically to OSN cilia but is largely excluded from the respiratory epithelium cilia in adult mice. Furthermore, we found that Q8BH53 expression begins around embryonic day E13.5 in the olfactory epithelium. We are currently using a knock-out mouse model to understand the functional role of Q8BH53 in the olfactory system. In addition, we are taking a biochemical approach to identify binding partners of Q8BH53 in OSN cilia. Acknowledgements: NIH DC007395

#P52 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Expression of Several Odorant Receptors Outside the Olfactory System

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Over one thousand G-protein coupled receptors have been classified as odorant receptors in the mouse genome based on sequence similarities with receptors found in the olfactory system. Recent studies have identified odorant receptors expressed outside of the olfactory system, and growing evidence supports a role for these receptors in extra-olfactory functions. We have examined expression of the odorant receptors M71, M72, I7, P2, MOR28, whose expression patterns have been well characterized in the olfactory system. We screened for expression of these receptors in extra-olfactory tissues by RT-PCR and then tested positive results by *in situ* hybridization, immunohistochemistry, or through the use of established reporter mouse lines. Identification of novel expression outside the olfactory system suggests a function for odorant receptors in these tissues. Future research will be aimed toward uncovering functions and identifying putative endogenous ligands. Acknowledgements: NIH DC007395

#P53 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

M3-R inhibits β-arrestin2 recruitment and desensitization of mammalian odorant receptors to potentiate their activation

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Adjusting sensitivity of sensory stimuli needed by an animal at any given time is crucial for animals' survival. In mammals, the activation of odorant receptors (ORs), which are expressed in the olfactory sensory neurons (OSNs) in the olfactory epithelium, mediates the perception of smell. These ORs belong to the large family of G protein-coupled receptors (GPCRs), which also include the muscarinic acetylcholine receptors that are key mediators of the parasympathetic nervous system output. Previously, we showed that activation of the muscarinic receptor M3-R has been shown to potentiate OR-mediated cAMP response, and the functional interaction between the M3-R and ORs suggests that odorant detection may be modulated by the neurotransmitter at the peripheral level. However, the mechanisms underlying this modulation were not understood.

Here we provide evidence suggesting that M3-R mediates the potentiation of OR signaling by inhibiting the recruitment of β-arrestin-2 to activated ORs. In line with this, activation of the M3-R by muscarinic agonist further inhibits β-arrestin-2 recruitment to ORs, while M3-R antagonist alleviates the inhibition. These effects are not explained by the competition for β-arrestin-2 between the two receptors. Further more, the third intracellular loop of the M3-R is responsible for its regulation of OR activity. This data suggests that the M3-R potentiates OR-mediated cAMP response largely by inhibiting the β-arrestin-2 recruitment to ORs, providing evidence for a novel mechanism of OR activity regulation by non-OR GPCRs, with β-arrestin-2 as a crucial mediator. Acknowledgements: This work is supported by grant from NIH.

#P54 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Off-flavor substances in foods and beverages cause a potent suppression of olfactory signal transduction

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We examined the effect of off-flavors in foods/beverages on the olfactory receptor cells under the whole-cell voltage clamp recording configuration. Generally, it has been shown that off-flavor substances induce exogenous unpleasant smells even with a very low concentration (ppt level inclusion in products). Although not yet scientifically demonstrated, it has also been pointed out that off-flavors reduce the pleasant flavors contained in foods/beverages. One of the most powerful off-flavors is 2,4,6-trichloroanisole (TCA), that is especially known for inducing the corktaint of wines. In the present study, we show with human psychophysical tests that TCA and related substances actually reduce flavors of foods and beverage with very low concentration. It was shown that TCA also suppressed cyclic nucleotide-gated (CNG) channels potently, when examined in olfactory sensory cilia. Surprisingly, the channel suppression was detected even when 1 aM of TCA was applied to the cell with an U-tube system. To explain such super-efficiency, the TCA effect showed the time-integration and slow recovery from the current suppression, presumably representing the integration of the substance into the hydrophobic site of the membrane. Based on the relation between the number of TCA molecules applied and total number of CNG channels, it was assumed that single TCA molecule may affect more than one CNG channel. This is also consistent with an idea that the effect of TCA is mediated by the lipid bilayer to affect surrounding channels simultaneously. TCA was found in a wide variety of foods/beverages, when screened out from their flavor losses. Natural generation of TCA and related off-flavor substances may be one of the mechanisms for the deterioration of those products.

#P55 **POSTER SESSION I: MULTIMODAL RECEPTION; CHEMOSENSATION AND DISEASE; OLFACTION PERIPHERY**

Effect of Vitamin A Deficiency on Olfactory Marker Protein Expression in Postnatal Mouse Olfactory Neurons

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Our lab has previously shown that Olfactory receptor neuron (ORN) levels decrease when sources of Vitamin A have been removed from the diet of postnatal rats. Experiments performed have been directed towards discovering whether or not the same results are observed in mice that were mutated with a lecithin retinyl acyl transferase (LRAT knockout, KO) gene. To determine the VAD effects on mice, specifically on ORN numbers we took LRAT KO male mice who were age-matched and fed them a VAD diet or a diet supplemented with VA (VAS) for 8 weeks (Study 1) or 19 weeks (Study 2). Studies included our control group, age matched, male wild type (WT) VAS mice. Our VAD rats exhibit distinct signs of VAD that include alopecia, ataxia, reddened eyes, white teeth and decreased weight gain relative to controls, LRAT KO mice did not display any of these signs after eight weeks on the VAD diet. LRAT KO mice on the VAD diet for 19 weeks showed a relative weight loss in the latter part of the study. Cytosolic extracts from Olfactory tissue were collected from mice in Study 2. Immunoblots were prepared and probed with an antibody directed against olfactory marker protein (OMP), a marker for mature ORNs. Chemiluminescent reagent detection system and images were acquired with a BioImaging System were used to evaluate relative OMP protein expression levels in LRAT KO VAD, LRAT KO VAS, and WT mice olfactory tissue cytosolic lysates. Signal area densities were recorded using an EpiChemi Darkroom UVP Bioimaging System. This allowed us to quantify the density of each band on the immunoblot. Results have shown that VAD mice have less OMP expression than those animals fed a VAS diet including the LRAT KO VAS mice and the WT mice. These findings suggest that VAD may have different and/or less pronounced effects on mice than rats. Acknowledgements: NIH/NIGMS/MBRS/ SCORE S06 GM 008092

#P56 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Cerebral processing of odors related to their hedonic judgment

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The aim of the study was to investigate parameters reflecting the hedonic component of odor perception. The emotional effect of smelling- claiming an odor as pleasant or unpleasant- is an important part of the central nervous connection of odor perception. It has been shown that perception of pleasant odors implicates different cerebral activations than that of unpleasant ones. Thirty-two healthy, right-handed subjects (16 men, 16

women; mean age 23.4 years; range 20-29 years) were examined. Normal olfactory function was ascertained using the "Sniffin Sticks". All subjects rated peach odor as pleasant, and the smell of butanol as unpleasant. According to their hedonic judgement of liquorice odor, subjects were divided into two groups: group 1 subjects described the odor of liquorice as pleasant, and group 2 subjects experienced liquorice as unpleasant. Functional magnetic resonance imaging (fMRI) was used to compare the cerebral activations while smelling the three different odors: pleasant peach, unpleasant butanol, and ambiguous liquorice. Analysis indicated common neural activations in response to all odors in a number of regions, e.g. in cingulate gyrus, medial frontal gyrus and caudate nucleus. In subjects disliking liquorice, activations were found in four areas including medial frontal gyrus, postcentral gyrus and medial temporal gyrus. In liquorice-liking subjects, activations were found in the medial frontal lobe. These results suggest that there are different patterns of central nervous activation dependent on the hedonic value of an odor, mainly including the frontal lobe, with unpleasant odors activating the more lateral frontal lobe and pleasant odors more medial areas. In addition, unpleasant odors produced more activation as compared to pleasant odors. Acknowledgements: Supported by Takasago, Paris.

#P57 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Valence Modulation of Crossmodal Olfactory-Visual Neural Integration

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We recently demonstrated that a concurring congruent visual stimulus does not affect olfactory sensitivity but does modulate the perceived valence or pleasantness and intensity of an odor. However, the congruency-dependent effect occurred only for odors perceived as pleasant. With the current study we explored the neural mechanisms of this behavioral phenomenon with the aim of determining the influence of valence on the neural correlates of crossmodal olfactory-visual integration. To this end, the pleasant odor phenyl ethyl alcohol and unpleasant odor isovaleric acid was applied using constant-flow olfactometry in combination with a congruent, incongruent, or blank visual stimulus during an event-related fMRI paradigm. As control stimuli we also applied pleasant and unpleasant visual stimuli and a baseline stimulus. We investigated brain activation due to crossmodal integration in 14 healthy, normosmic participants. Subjects had to rate pleasantness of the odors after each event. Statistical analyses of the behavioral data demonstrate a replication of the aforementioned findings. As predicted, valence-independent olfactory-visual integration was mediated by low-level multisensory integration areas in the superior parietal lobule. Preliminary analyses of the fMRI data indicate that valence-dependent integration occurs in higher-order multisensory integration areas in conjunction with areas known to code for odor valence. Moreover, a differential processing of unpleasant compared to pleasant olfactory-visual stimulus combinations has been established. Further insights into the neural processes mediating the influence of valence on the neural correlates of olfactory-visual integration will be discussed. Acknowledgements: Funded by a startup grant from the Medical Faculty of RWTH Aachen University.

#P58 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Visuo-olfactory integration facilitates peri-threshold olfactory categorization

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Olfactory quality discrimination and categorization proves a highly challenging process in humans. Additional information from other senses, such as visual cues, may facilitate this operation via crossmodal integration. To date, crossmodal sensory integration has focused on non-chemical senses. Using functional magnetic resonance imaging (fMRI) techniques, this study characterized visuo-olfactory integration in olfactory categorization. Participants (N=29) smelled an odor at a merely detectable level from one of three categories (food, floral, or wood) while viewing a picture that was congruent or incongruent to the odor, and then made a category decision on the odor. Reaction time (RT) was faster for congruent versus incongruent stimuli (P<.05). Similarly, accuracy was higher for congruent than incongruent stimuli (P's<.005). These results reveal effective visuo-olfactory integration in improving otherwise chance-level odor quality categorization. fMRI analysis demonstrated enhanced right olfactory orbitofrontal cortex (oOFC) response to congruent versus incongruent visuo-olfactory pairing, for all three odor categories. Importantly, this enhancement in oOFC was strongly associated with congruency-related improvement in odor categorization (in RT and accuracy). Our findings suggest that despite the peri-threshold level of odor presentation and consequent difficulty in odor categorization, visual input can be integrated with olfactory information and markedly improve this process. In particular, the secondary olfactory cortex in the OFC mediates this process, presumably via its highly associative multimodal connections. Multi-voxel pattern analysis is underway to examine nuanced quality representation by ensemble neuronal activity in the primary (piriform) and secondary (oOFC) olfactory cortices. Acknowledgements: Funding supported by R01MH093413 (W.L.), P30HD03352 (W.L.)

#P59 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

The chemosensory path of pain

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The function of the olfactory system has been well investigated over the last decades. However, we know much less regarding central processing of intranasal trigeminal stimuli. Trigeminal sensations like burning, stinging, tingling, pungency and temperature constitute an additional quality in perception of odor and flavor, but also allow odor localization in contrast to pure olfactory odors. In this study we focused on three different trigeminal compounds which target various sensory receptors and produce distinctive sensations: CO_2 elicits stinging sensations (activating TRPV1 receptors), cinnamaldehyde burning sensations (TRPA1) and menthol cooling sensations (TRPM8). The point of interest was to investigate discrepancies in the processing of different intranasal chemosensory trigeminal stimulations along the trigeminal pathway. Moreover, we aimed to reveal activation in olfactory areas which supports a close relationship between the two chemosensory systems.
We conducted an fMRI study on a 3T MRI scanner to measure neural activity in 12 healthy subjects. Each of the three stimuli was delivered separately by a computer-controlled air-dilution olfactometer in one session. Using an event-related design subjects received trigeminal stimuli of 500ms to the left nostril (ISI 30s). During the whole experiment subjects were asked to breathe using velopharyngeal closure. Functional imaging data were analyzed with Independent Component Analysis. Insula, SI and OFC were activated by all three compounds. Further, all three conditions led to activation of the PFC demonstrating the well established interaction between the olfactory and trigeminal system. The findings support the notion that activation of the three trigeminal receptors is processed in the same pathway.
Acknowledgements: FWF (P23205-B09)

#P60 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

Smell what you seek – Reward sensitivity amplifies visuo-olfactory integration of positive affect

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Crossmodal integration is a process ubiquitous in animals with multiple sensory systems, facilitating perception especially when challenged with limited stimulus input. However, there is little research on integration of positive affect, still less how this process varies with relevant individual differences such as reward sensitivity. Reward sensitivity may increase response to rewarding stimuli, thereby facilitating crossmodal integration of positive affect. Applying functional magnetic resonance imaging (fMRI) techniques, this study examined visual and olfactory integration of reward. Participants (N=29) performed an odor categorization task: they smelled an odor from one of two categories (floral or wood) while viewing an image congruent or incongruent with the odor, followed by a category decision. Reaction time was faster and accuracy greater for floral than wood odors (P's<.005), and accuracy was greater for congruent than incongruent trials (P<.005), suggesting preferential response to pleasant and bimodal stimulation. fMRI analysis demonstrated enhanced left amygdala and hippocampus activation for floral than wood odors and congruent than incongruent trials. Although behavioral response was not associated with reward sensitivity as measured by the Behavioral Activation Scale (BAS), positive affective and integrative responses in right amygdala, hippocampus, and piriform cortex were greater with higher BAS scores, especially in fun-seeking. The amygdala and hippocampus are key contributors in the reward circuitry in the brain, projecting to ventral striatum and triggering downstream processes driving reward experience. Higher reward sensitivity thus promotes reward processing by facilitating integrative processing of pleasant sensory inputs in both limbic and primary sensory regions. Acknowledgements: R01MH093413 (W.L.) and P30HD03352 (W.L.)

#P61 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

Biochemical components of trigeminal integration in anosmics: A pilot functional magnetic spectroscopy study

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Several studies investigated functional interaction of the olfactory and trigeminal system. Although anosmic patients are not able to perceive odors they show changes in "insular" blood oxygenation during trigeminal neuronal activity. This pilot study aimed to investigate how changes on blood oxygenation level, as observed by fMRI, are underlined by changes in neurotransmitter (GABA, glutamate) balance under trigeminal simulation in the insula and how these changes differ between anosmic and healthy populations. 3 (2f;25-43ys) functional anosmics and 8 controls (6f;18-43ys) were examined using proton magnetic resonance spectroscopy (1H-MRS) to explore changes of excitatory and inhibitory neurotransmitters in the insula. Spin-echo based MRS (TE=30ms/TR=5000ms) measurements were performed on a 3T whole body MR scanner, using a 32ch coil for signal detection combined with a stimulation device, which was designed specifically for intranasal application. The paradigm consisted of 4 stimulation blocks: 4 dynamic cycles with 32 acquisitions, and 32 stimuli (CO_2, 50%v/v, birhinal, 250ms). Acquired spectral transients were individually frequency corrected, phased and further grouped according to the timeline position into baseline- and stimulation-groups. The quantification of metabolic intensities was performed using the LCModel with an imported modelled basis set including metabolites and macromolecular resonances. Results for controls revealed decreased GABA (41.24%) during the rest phase. Anosmic patients showed a significant decrease of glutamate (16.42%) and a higher GABA response (205.25%) rate to stimulation compared to controls. Results of this study will significantly contribute to the basic understanding of trigeminal processing of chemosensory information in patients with olfactory dysfunction. Acknowledgements: FWF (P23205-B09)

#P62 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

Superadditive processing during flavor perception is modulated by anterior temporal cortex connectivity

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The combination of taste and odor found in a flavorful dish creates a more powerful sensation than its odor or taste in isolation. Whereas the neural processing of the individual chemosensory components is well known, the functional connectivity underlying the combined flavor percept is poorly understood. In the present functional magnetic resonance imaging study, subjects were presented with taste only (gustatory presentation of juice, closed soft palate), smell only (orthonasal presentation of juice odor), or a combined flavor (retronasal-gustatory presentation, swallowing juice). As expected, olfactory stimulation alone activated olfactory areas while gustatory stimulation alone elicited activation within the gustatory cortex. Overlapping activation within both networks could be observed during flavor presentation, and a convergence zone between all three conditions was observed in the anterior ventral insula and cingulate cortex. Superadditive activity for the flavor condition, relative to odor and taste alone, was observed in the dorsal insular gyrus, extending into parietal operculum and postcentral gyrus. Finally, to delineate the cerebral networks contributing to the flavor percept, we assessed the functional connectivity between these significant nodes responsive to chemosensory overlap during combined odor-taste stimulation. Increases in functional connectivity with both convergent and superadditive areas were observed in an overlapping area in the temporal pole. Taken together, these findings are suggestive of an important relay function of semantic memory circuits in the formation of the flavor experience from crossmodal chemosensory information.

#P63 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

Is the Superior Temporal Sulcus involved in the Reinforced Configural Processing of a Binary Odor Mixture?

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In macaque monkeys the superior temporal sulcus (STS) projects to the orbitofrontal cortex which projects to the primary olfactory cortex (Carmichael and Price 1995). These connections are believed to be reciprocal, therefore the STS is supposed to receive inputs from olfactory areas. Kettenmann et al. (1996) showed that STS was activated when participants were stimulated with monomolecular odors. This area is also specifically activated for configural visual processing, as during the perception of body motion (Thompson et al. 2005). In the present study, we investigated the configural processing of odor mixtures in human adults. We repeatedly exposed (2 sessions of 11 exposures) healthy volunteers (n=12, G_{AB}) to a binary mixture (AB) configurally processed (blending of the two components' odors into a single pineapple odor), while others (n=14, G_{compo}) were exposed to the separate components, A ("strawberry") and B ("caramel"). To equilibrate the number of exposures in the two groups, G_{AB} was also exposed to PEA (monomolecular, "rose"). Such exposures were known to favor the perception of the AB configuration in G_{AB} and the perception of the elements in G_{compo} (Sinding et al. 2011, in preparation). Two days after the pre-exposure, all subjects received an fMRI while stimulated by AB, A, B and PEA. As a major result, the STS appeared significantly more activated for the processing of the AB mixture in G_{AB} than in G_{compo}. The STS was also more activated for the processing of AB as compared to A and B, in G_{AB}. The STS was not significantly activated in G_{compo} for any stimulation, in any contrast. These results suggest that the STS is a critical area for the reinforced configural processing of simple odorant mixtures. However, PEA also activated significantly the STS in G_{AB} in comparison to G_{compo}. Acknowledgements: Supported by grants from the Burgundy Regional council and EU-ERDF to GC and TTD, European Dijon-Dresden Laboratory (LEA 549) to TH, GC, TTD, and a fellowship from the French MESR to CS.

#P64 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

Association of Pleasantness and Intensity of Sweet and Salty Taste in the Human Brain

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An abnormal assessment of pleasantness and intensity of tastants can lead to negative, long-term health conditions. Among these, obesity may be a consequence of diminished sensitivity to sweet tastes, leading to amplified cravings and associated weight gains. An understanding of the neural processes of taste perception is essential for elucidating this disease state. Unfortunately, studies on the human brain are limited, and thus the majority of neural taste function knowledge stems from animal studies. These studies have shown that hedonic and intensity information is encoded in the primary gustatory cortex, with neuronal firing correlated with stimulation intensity. Seeking to confirm animal models in the human brain, this study utilized fMRI to study BOLD signal changes in response to varied concentrations of sweet and salty taste stimulants. Normal, healthy volunteers (n=11) completed a total of fifteen taste fMRI studies in which brain response to an event-related taste stimulation paradigm was correlated with perceived ratings of both pleasantness and intensity. The data indicate a positive correlation between pleasantness and intensity for sweet tastants; while a negative correlation was observed for salty tastants. Each triggered significant activation in the primary and secondary gustatory cortices including: bilateral anterior insular cortex, posterior orbitofrontal cortex, cingulated cortex, and dorsolateral prefrontal cortex. BOLD signals in these regions were significantly correlated with both hedonic and intensity ratings from subjects. Overall these results show that the human brain processes hedonic and intensity information of sweet and salty taste through similar neural networks previously seen in animal models.

#P65 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

Perception and encoding of odor elements and mixtures in the human brain

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In the natural environment, most odorous objects are composed of dozens, if not hundreds, of volatile molecules. Despite this apparent complexity, the olfactory system seamlessly integrates these components into perceptual wholes. Utilizing a between subject design, this experiment aimed to investigate how experience in the form of aversive learning modulates perception and encoding of odor mixtures by pairing either a target binary odor mixture (Mx) or one of its components (Ele) with an electric shock. We used psychophysical measurements, functional magnetic resonance imaging (fMRI), and multivariate analytical techniques to investigate these learning induced changes. We presented human subjects with six stimuli: three monomolecular odorants (A, B, C), and three binary mixtures (AB, BC, AC). To date, results have been collected for 13 subjects (8 Ele, 5 Mx) who were successfully conditioned. When asked to identify the odor component(s) of these stimuli, subjects in the Mx group showed decreased accuracy in identifying the correct component(s). Moreover, these subjects also rated mixtures to be less similar to their components, while subjects in the Ele group rated mixtures to be more similar to their components after conditioning. These preliminary findings suggest that olfactory learning of a binary mixture may induce perceptual and neural fusion of odor elements into a synthetic whole. Conversely, pairing a shock with a component of a binary mixture may induce neural "fission" of the mixture, such that its components are processed in a more elemental fashion. Ongoing fMRI analysis will test the hypothesis that learning induced changes in odor quality perception may be reflected in the correlation between odor evoked patterns of activation in the posterior piriform cortex. Acknowledgements: This work was supported by Northwestern Institutional Predoctoral Training Awards to K.N.W. (T32NS047987) and grants R01DC010014 and K08DC007653 from the US National Institute on Deafness and Other Communication Disorders to J.A.G.

#P66 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

The Fate of the Inner Nose: Odor Imagery in Patients With Olfactory Loss

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Although the concept of olfactory mental imagery remains controversial, recent studies support the principle. Cerebral activations during olfactory mental imagery are fairly well investigated in healthy participants but very few studies address the subjects of olfactory imagery in patients with olfactory loss. To investigate if olfactory imagery is impaired in patients who are no longer able to smell, 16 participants with acquired anosmia and 19 normosmic control participants have been investigated. We used functional magnet resonance tomography and subjective ratings to explore the mechanisms during mental imagery of odors. After an imagery training, participants imagined odors triggered by words naming pleasant and unpleasant olfactory objects. We found that the patients compared to healthy control participants showed greater difficulties in imagining odors and lower intensity scores while doing so. Looking at neural activation, the pattern observed by Bensafi et al. (2007) that imagining unpleasant odors leads to more activation in olfaction-related areas than imagining pleasant odors was found in the control group but not in the anosmic group. This hedonic specific approach was meant to control for activation that was due to attention allocation or activation of semantic circuits that are alone sufficient to evoke activation in olfactory areas. Direct comparisons between the groups revealed greater activation in the anosmic group in olfactory areas than in the control group. We conclude that, in contrast to the control group, anosmic participants have difficulties to perform olfactory imagery in the conventional meaning.

#P67 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

Multi-modal functional imaging of rat olfactory bulb with orthonasal and retronasal odorant stimulation: functional insights through complementary techniques

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Various techniques can be used to evaluate odor response maps of the olfactory bulb, each with its own advantages. Here we combined fMRI with intrinsic and calcium optical imaging to

better characterize glomerular responses. Functional MRI and intrinsic imaging share slow responses of complex origin which are based on dynamic changes in oxy- and deoxy-hemoglobin. Whereas fMRI can image the entire bulb, intrinsic and calcium are limited to the dorsal regions but with high spatiotemporal resolution. CBV-weighted fMRI was unsuccessful in bulb imaging, as was the use of other anesthetics (Ex:domitor). In seven rats we performed micro fMRI (BOLD, 120x120x300µm) in dorsal orientation so that data could be compared to subsequent calcium imaging of orthonasal responses in the same subjects. In a few cases odor induced activation maps showed strong overlap between the two imaging modalities. We further apply these techniques in separate animals to define retronasal dorsal and whole bulb responses and compare those to orthonasal odorant presentations. We have found significant effects of odor route on the response magnitude and timing. Further, retronasal odor concentration affects response latency in a direction depending on the odorant. We are evaluating several methods of post-hoc co-registering across these methods 1) across functional maps (fMRI, intrinsic, calcium), 2) using phantom markers on the skull, 3) using vasculature via venogram MRI, and 4) using SWIFT-MRI for skull imaging. Due to the partial volume effect and the relatively thin dorsal glomerular layer we are also developing a miniature phased coil-array allowing higher resolution and high quality dorsal functional images. Our comparative approach shows the challenges in obtaining and interpreting odor maps using different methodologies. Acknowledgements: This work is supported by NIH/NIDCD Grants R01DC009994 and R01DC011286.

#P68 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Quantifying Bursting Olfactory Neuron Activity from Calcium Signals Using Maximum Entropy Deconvolution

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Advances in calcium imaging have enabled studies of the activity dynamics of both individual neurons and neuronal assemblies. However, inferring action potentials (spikes) from calcium signals is still a challenging issue due to hidden nonlinearity in their relationship, contamination by noise, and often the relatively low temporal resolution of the calcium signal compared to the time-scale of spike generation. Complex neuronal discharge, as in the case of the bursting or rhythmically active neuronal activity represents an even greater challenge for reconstructing spike trains based on calcium signals. Here we propose doing this using blind calcium signal deconvolution based on a theoretical information approach. The basic idea is to maximize the output entropy of a nonlinear filter where the nonlinearity is defined by the cumulative distribution function of the spike signal. We tested this maximum entropy (ME) algorithm on bursting olfactory receptor neurons (bORNs) in the lobster olfactory organ. The advantage of the ME algorithm is that the filter can be trained online based only on the statistics of the spike signal without making any assumptions about the spike-calcium signal relation. We show that the ME method is able to reconstruct the timing of the first and the last spike of a burst with higher accuracy compared to other methods. Thus the ME method should be a useful tool for inferring parameters of bursting neurons, including bursting olfactory neurons, to help further understand the mechanism and function of bursting-based neuronal sensory coding. Acknowledgements: Supported by award R21 DC011859 from the NIDCD

#P69 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Allometric Growth of Olfactory Bulb and Brain in Female Minks

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The olfactory bulb is the anterior part of the brain and phylogenetically one of the oldest brain structures. During postnatal development, when the animal grows, the brain increases in size – and so does the olfactory bulb. However, in some mammals, such as the American mink (*Neovison vison*) it is known, that brain shows an overshoot development postnatally with a subsequent reduction in size. Thus we were interested, if this applies also to the olfactory bulb. Therefore we analyzed morphometrically a total of 57 female minks ranging from newborn (postnatal day 0, P0) to one year of age for their brain and olfactory bulb size. The results reveal, that the volume of one olfactory bulb in newborns is 1.26 ± 0.02 mm^3, increasing continuously (P30: 40.27 ± 8.77 mm^3; P90: 84.70 ± 1.87 mm^3) to adult values (107.19 ± 4.15 mm^3) with no overshoot phenomena. In contrast, the brain weight increases postnatally from P0 (0.29 ± 0.06 g) up to P90 (10.18 ± 0.42 g) when maximal values are reached, and decreasing afterwards more than 17% to the adult size (8.43 ± 0.35 g). The olfactory bulb growth therefore does not parallel the total brain growth but shows an allometric growth pattern. On the other hand, the overall body growth increases continuously to adult values resulting in an olfactory bulb/body weight ratio of similar values among newborns, brain overshoot age and adults (P0: 0.014±0.002 %; P90: 0.012±0.002 %, adult: 0.011±0.001 %) with higher values early postnatally (P30: 0.047±0.013 %). This indicates that the olfactory bulb is influenced by other factors than the cortical neurons for its neuronal network growth and controlled by different stimuli for its formation and connectivity. Further, no postnatal reduction in size suggests a basic and important functional relevance of the olfactory bulb.

#P70 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Effect of kamikihito (TJ-137) on nerve growth factor and olfactory nerve *in vivo*

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Background: A Kampo product, kamikihito (product name code: TJ-137), has ingredients that promote nerve growth. Paclitaxel, a cancer chemotherapeutic agent, is toxic to olfactory nerve cells *in vivo*. To show TJ-137 pre-medication effect on nerve growth factor (NGF) in olfactory bulb and paclitaxel induced olfactory neuropathy *in vivo*. Methods: Female 7-week-old Bulb/c mice were fed food containing TJ-137, or control food, for 14 days before and after intravenous paclitaxel administration. NGF was assessed with ELISA in the olfactory bulb of mice fed food containing TJ-137 (n=9), or control food (n=9) for 14 days. The epithelial changes in the nasal turbinates of mice were assessed by H&E and immunohistochemical staining for the olfactory marker protein (OMP). The accumulation of the neuronal tracer (Dextran tetramethylrhodamine) in the olfactory bulb was assessed in frozen sections of mice 48 h after nasal administration of the tracer. Results: NGF was significantly increased in the olfactory bulb of mice fed food-containing TJ-137 than in the control mice (P=0.017). The epithelium of nasal turbinates of TJ-137 treated mice was less injured than that of the control mice after paclitaxel administration. The accumulation of the neuronal tracer in the olfactory bulb was higher in the TJ-137 treated mice compared to controls. Conclusion: We found that TJ-137 is effective in increasing NGF in olfactory bulb and reducing paclitaxel induced olfactory neuropathy *in vivo*. Acknowledgements: Assist Kaken from Kanazawa Medical University (2012)

#P71 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Fgf8 Defines Neurogenic Vomeronasal and GnRH Neurogenic Mileu by Influencing BMP and BMP Antagonists Expression.

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FGF8 plays a pivotal role in development of craniofacial structures, the olfactory/vomeronasal system and GnRH neurons. BMPs can antagonize FGFs expression and signal, BMP and FGF8 signaling are known to exert opposite roles in defining epithelial versus neurogenic fate. We analyzed the relation between Fgf8, BMP and BMP anatgonists in the developing olfactory pit in two Fgf8 hypomorph mouse models, expressing different levels of FGF8. In both mutant mouse models, $Fgf8^{neo/neo}$and $Fgf8^{neo/Null}$, regardless of the FGF8 dosage, overlapping defects were observed in the olfactory pit: lack of neurons formation limited to the ventral area of the developing nasal pit and the proximal portion of respiratory epithelium, where GnRH neurons normally form. Analyzing expression of BMP4 and BMP antagonist Noggin we found a previously not described large mesenchymal Noggin source that sharply defines a BMP free GnRH and VNO neurogenic border. In Fgf8 hypomorphs BMP4 and Noggin expression were found to be altered, with Noggin no longer defining the GnRH and VNO neurogenic border. These data suggest that the role played by FGF8 in controlling cell fate specification and neural patterning of the olfactory pit is in large part indirect as Fgf8 levels affect both BMP and Noggin expression in the pit and nasal mesenchyme. BMP and Noggin expression respectively define the epithelial or neurogenic permissive borders. The previously described lack of GnRH neuron specification in animals with chronically reduced FGF8 reflects the loss of a large neurogenic permissive milieu that includes the entire VNO. Acknowledgements: The work presented was supported by the Intramural Research Program of the National Institutes of Health, National Institute of Neurological Disorders and Stroke

#P72 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

An IP3R3- and NPY-expressing microvillous cell mediates tissue homeostasis and regeneration

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Calcium-dependent release of neurotrophic factors plays an important role in the maintenance of neurons, yet the release mechanisms are understudied. The inositol triphosphate (IP3) receptor is a calcium release channel that has a physiological role in development, sensory perception, neuronal signaling and secretion. In the olfactory system, the IP3 receptor subtype 3 (IP3R3) is expressed exclusively in a microvillous cell subtype that is the predominant cell that expresses neurotrophic factor neuropeptide Y (NPY). We hypothesized that the IP3R3-expressing microvillous cells secrete sufficient NPY needed for both the continual maintenance of the neuronal population and for neuroregeneration following injury. We addressed this question by assessing the release of neurotrophic factor NPY and regenerative capabilities in wild type mice, $IP3R3^{+/-}$, and $IP3R3^{-/-}$ mice. Injury, simulated using extracellular ATP as a model, induced IP3 receptor-mediated NPY release in wild-type mice. ATP-evoked NPY release was impaired in $IP3R3^{-/-}$ mice, suggesting that IP3R3 contributes to NPY release following injury. Under normal physiological conditions, both $IP3R3^{-/-}$ mice and explants from these mice had fewer progenitor cells that proliferate and differentiate into immature neurons. Although the number of mature neurons and the in vivo rate of proliferation were not altered, the proliferative response to the

olfactotoxicant satratoxin G and olfactory bulb ablation injury was compromised in the olfactory epithelium of IP3R3$^{-/-}$ mice. The reductions in both NPY release and number of progenitor cells in IP3R3$^{-/-}$ mice point to a role of the IP3R3 in tissue homeostasis and neuroregeneration. Collectively, these data suggest that IP3R3 expressing microvillous cells are actively responsive to injury and promote recovery. Acknowledgements: Supported by NIH DC006897 (CCH), MSU institutional funds (CCH), NIEHS T32 ES007255 (CRH), NINDS T32 NS044928 (AEP and TRI) and Swiss Fellowship for Advanced Researchers PA 00P3_131493 (SH).

#P73 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

PACAP increases $[Ca^{2+}]_i$ in neonatal OB via direct and indirect mechanisms

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Our lab has been studying the pleiotropic peptide named Pituitary Adenylate Cyclase Activating Peptide (PACAP) in the olfactory epithelium[1] of rodents. The physiological effects of PACAP in the olfactory bulb (OB) are still unknown. Neonatal OB is enriched with both PACAP and its G-protein coupled receptor PAC1R. Without PACAP, neonates often die before weaning, suggesting that PACAP is required for normal development. Previously, we showed that PACAP led to an oscillating increase in $[Ca^{2+}]_i$ in OB neurons. To address whether the PACAP-induced responses are direct or indirect, we used cocktails of antagonists for the GABA receptors (GABAR) and/or glutamate receptors (GlutR) in the presence and absence of PACAP. We performed confocal Ca^{2+} imaging on live slices from P2-P5 mice loaded with the Ca^{2+} indicator dye Fluo-4 AM. The optimal dose of PACAP was empirically determined to be 40 nM and was used in all experiments. Combined block of GABAR and GlutR yielded a 66% decrease in numbers of PACAP responsive cells. Blocking just GlutR resulted in a similar reduction, suggesting that glutamate mediates the majority of the indirect effects. Interestingly, blocking only the GABAR resulted in block of GABA-induced initial Ca^{2+} response on immature cells. However, the majority of these cells showed the post-PACAP oscillation. Our data suggest 1) about 1/3 of the PACAP-responsive cells have direct PAC1R activity. 2) PACAP promotes glutamate release which in turn activates 2/3 of the PACAP-responsive cells. 3) GlutR may have a role in the post-PACAP $[Ca^{2+}]$ oscillation. 4) GABA is also released by PACAP from PAC1R-rich GABAergic cells. In conclusion, we find that PACAP has both direct and indirect effects on neonatal OB neurons and may promote glutamate and GABA release in early development. Acknowledgements: NIH 1F31DC011686-02 Blackman Trust Fund 00253 6000 16917 University of Utah Graduate Research Fellowship 2011

#P74 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Inactivation of the Interoceptive Insula Suppresses Chemosensory Cue Reactivity to Ethanol Following Chronic Ethanol Exposure

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Recent findings indicate that the insular cortex is critically involved in addictive behavior to multiple drugs of abuse by regulating an organism's responsiveness to drug-associated sensory cues. Damage to the insula in addicted smokers results in a disruption of nicotine addiction, and inactivation of the insula in rodents disrupts conditioned preference for environments previously paired with amphetamine or nicotine. Imaging studies have demonstrated activation in the insula during drug craving and exposure to drug-related cues, including the taste of alcohol in heavy drinkers. The present study measured chemosensory responses to ethanol in chronically ethanol-exposed or naive rats under conditions of pharmacological silencing of the visceral insula to examine the role of this brain region in mediating responses to ethanol-associated sensory cues. Rats were initially exposed to either a 20% ethanol intermittent access paradigm or were given access only to water. Following implantation of intracranial cannulae, rats from each exposure condition were tested for brief-access lick responses to ethanol (0-40%) after receiving bilateral insula infusions of saline or muscimol. Alcohol-experienced rats displayed a concentration-dependent increase in chemosensory avidity for ethanol compared to alcohol-naive rats, evidenced by elevated lick responses and trial sampling frequency particularly at higher ethanol concentrations (15-40%). Inactivation of the insula eliminated this concentration-dependent response in chronically exposed animals, but did not modify orosensory responses to ethanol in alcohol-naive rats. These data support insular cortex involvement in mediating responsiveness to conditioned alcohol chemosensory cues following chronic association of ethanol's taste and post-absorptive effects. Acknowledgements: Support Contributed By: NIH AA015741

#P75 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Growth patterns of sensory neuron axon terminals in the developing olfactory bulb

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The developing, but also the mature vertebrate olfactory system is a site of ongoing neurogenesis. Olfactory stem cells continuously generate new sensory neurons which extend

axons into the olfactory bulb where they face the challenge to integrate into an existing neuronal circuitry. Synaptic contacts to second-order neurons are formed in distinct target regions, so-called glomeruli. In rodents, sensory neurons normally project only into one specific glomerulus of the olfactory bulb. We investigated the growth patterns of sensory neuron axons in the developing olfactory system of the aquatic amphibian *Xenopus laevis*. To address the question how connectivity is reshaped during olfactory system maturation a range of larval stages and young postmetamorphic animals were included in the experiments. Fluophore-coupled dextrans or plasmid DNA, encoding for fluorescent proteins, were introduced into sensory neurons via electroporation. The main sensory projection fields within the main- and accessory olfactory bulb were visualized by electroporation of the whole olfactory organ. During metamorphosis the main olfactory system is completely reorganized, whereas the sensory neurons of the accessory olfactory system are maintained. The axonal branching patterns of sensory neurons, originating from both the vomeronasal and main olfactory epithelium, were investigated by sparse staining of sensory neurons. Synaptic connections were clearly visible as tufted axonal endings. Most sensory neurons showed a branched axonal pattern before terminating in tufted arborizations inside glomeruli. Surprisingly, a high percentage of cells terminated in multiple and not single glomerulus-like structures. This pattern was comparable in sensory neurons originating from both the vomeronasal and the main olfactory organ. Acknowledgements: Supported by DFG Cluster of Excellence "Nanoscale Microscopy and Molecular Physiology of the Brain" (CNMPB) to I.M. and DFG Schwerpunktprogramm 1392 to I.M.

#P76 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Activity-Dependent Expression of Odorant Receptors in the Mouse Olfactory Epithelium

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Sensory experience plays critical roles in development and maintenance of the olfactory system, which undergoes considerable neurogenesis throughout life. In the mouse olfactory epithelium, each primary olfactory sensory neuron (OSN) stably expresses a single odorant receptor (OR) type out of a repertoire of ~1200. All OSNs with the same OR identity are distributed within one of the few broadly-defined zones. However, it remains elusive whether such OR expression patterns are shaped by sensory stimulation and/or neuronal activity. Here we addressed this question by investigating OR gene or protein expression in two surgically- or genetically-modified mouse models. Using in situ hybridization, we examined the expression patterns of 15 selected OR genes in mice which underwent neonatal, unilateral naris closure. After four-week occlusion, the expression level in the closed side was significantly lower (for four ORs), similar (for three ORs) or significantly higher (for eight ORs) than that in the open side. In addition, using a specific OR antibody, we demonstrated that this OR protein was upregulated in the closed side but downregulated in the open side. Furthermore, we examined the expression patterns of individual OR genes in transgenic mice in which olfactory marker protein (OMP) drives overexpression of the inward rectifying potassium channel (Kir2.1) in most mature OSNs to reduce their neuronal activity. The cell density for most OR genes (six out of seven tested) was significantly reduced compared to wild-type controls. The results suggest that sensory inputs have differential influence on OSNs expressing different ORs and that neuronal activity is critical for survival of OSNs. Acknowledgements: Supported by grants from the NIDCD/NIH DC006213 and DC011554.

#P77 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Optogenetic Investigation of GABAergic Circuitries in the Rostral Nucleus of the Solitary Tract

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The rostral nucleus of the solitary tract (rNTS) is the first central target of primary gustatory nerve fibers and as such plays an essential role in the processing and coding of peripheral taste sensory information. The intrinsic circuitry within rNTS is likely integral in shaping the incoming information into both ascending and descending efferent signals. Substantial subpopulations of interneurons in the rNTS are GABAergic and thus contribute to the generation of hyperpolarization-activated changes in repetitive firing patterns in projection neurons. Despite this importance in shaping rNTS gustatory-evoked signaling, the organization of rNTS GABAergic circuits is unknown. To investigate the organization of GABAergic innervation onto identified populations of neurons, we used a mouse model in which channelrhodopsin was expressed under the control of the vesicular GABA transporter. GABAergic interneurons were activated in an in vitro slice preparation with 473 nm laser illumination merged into the optic train of the microscope. Focused laser illumination produced consistent saturated photocurrents in GABAergic neurons with high temporal and spatial resolution. While recording inhibitory postsynaptic currents in either GABAergic or non-GABAergic neurons, the laser spot was systematically scanned over discrete portions of the rNTS to map out the GABAergic innervation onto the recorded neuron. Neurons received inhibitory innervation from wide expanses of rNTS, often with focal spots of strong inhibition located in areas not immediately adjacent to the recorded neuron. This suggests that in addition to a low level of global inhibition, there are also specific subregions of rNTS that are able to strongly hyperpolarize individual neurons and possibly induce alterations in repetitive discharge patterns. Acknowledgements: T32DC000011, RO1DC000288

#P78 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Sensory Afferents from the Stomach of the Rat Converge onto Taste-responsive Neurons in the Rat Brainstem

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Recent descriptions of taste receptors in the gut have set the stage for the idea that taste stimuli continue to provide information even when they are no longer in the mouth. For example, intraduodenal infusions of bitter tastants can modify eating behavior within a single meal. Given that both taste and post-lingual chemosensory feedback may be important for modifying eating behavior on a relatively short timescale, it is possible that chemosensory afferents from the gut may converge onto the same relay nuclei as taste information in the brainstem. We investigated the responsiveness of single neurons in the rat brainstem to tongue and gastric taste stimulation. Initially, rats were anesthetized with urethane and prepared for recording from the brainstem. A length of polyethylene tubing was threaded down the rat's esophagus to the stomach for delivery of tastants. A tungsten microelectrode was then placed in the nucleus of the solitary tract (NTS) and taste-responsive cells were isolated. Preliminary data from 18 taste-responsive cells show that some (n=8) NTS cells change their firing rate in response to infusion of small amounts (0.4 ml) of taste stimuli (0.1 M NaCl, 0.01 M HCl, 0.01 M quinine, 0.5 M sucrose and 0.1 M MSG) into the stomach. Gastric responses were most frequently found to NaCl and MSG; no excitatory responses were found to HCl infused into the stomach. An additional cell was not responsive to lingual taste stimuli but was inhibited by gastric tastant delivery of MSG, HCl and quinine. Collectively, these data suggest that information from both lingual and post-lingual chemoreceptors converge onto NTS cells, suggesting a role for post-lingual chemoreceptors in modulation of ingestive behavior on a short timescale. Acknowledgements: Supported by NIDCD grant RO1DC006914 to PMD.

#P79 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Synaptic Properties of the Basolateral Amygdala Projection to Gustatory Cortex

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The gustatory cortex (GC) receives a dense and anatomically well documented projection from the basolateral nucleus of the amygdala (BLA). This input is thought to convey affective and anticipatory information regarding taste. Indeed inactivation of BLA results in dramatic changes in the way taste and anticipatory cues are processed in GC. Although the behavioral and functional significance of this projection has been the focus of extensive investigation in awake and anesthetized animals, the synaptic properties and organization of these inputs are unknown. To study the BLA to GC synapse, viral vectors carrying a construct for ChannelRhodopsin2 were injected in the BLA. After 2 weeks, whole-cell recordings in dysgranular and agranular GC were performed in combination with photoactivation of BLA terminal fields. BLA afferents were found to target both excitatory and inhibitory neurons in all layers of GC. Across all layers, approximately 60% of regular-spiking (RS), fast-spiking (FS), and low-threshold spiking (LTS) neurons responded to light-activation of BLA afferents. RS cells had a longer rise time than FS cells (p=.016) and a longer decay time than FS cells (p=.0004). In addition, differences could be seen in the synaptic properties of BLA inputs onto neurons in superficial and deep layers of GC. Layer 2/3 RS cells had larger current amplitudes than layer 5/6 cells (p=.03), and there was a significant difference in the percentage of FS cells that responded to stimulation in layer 2/3 (75%) and layer 5/6 (25%). These data suggest that BLA inputs in GC have cell type specific and layer specific properties. The combination of feed-forward inhibition and excitation likely serves to shape the temporal dynamics of taste responses and to enhance the representation of behaviorally salient stimuli. Acknowledgements: National Eye Institute Grant #R01-EY019885-S1 and National Institute on Deafness and Other Communication Disorders Grant #R01-DC010389

#P80 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Cortical modulation of taste-related orofacial behaviors

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Upon receiving a taste stimulus, primates and rodents produce a sequence of rhythmic orofacial movements, also known as taste reactivity (TR), specific elements of which reflect the hedonic quality (i. e., the palatability) of the stimulus. Aversive stimuli, such as quinine, elicit bouts of gapes, movements that serve to eject the stimulus from the mouth. The production of gapes indicates aversiveness, and the latency to gape is inversely related to the degree of aversiveness (Travers and Norgren, 1986). While the motor circuits necessary for taste-related orofacial movements are contained within a brainstem network (Grill & Norgren), in the intact animal, this network is modulated by feedback from higher-order forebrain structures. Relatively little is known about forebrain structures' roles in the selection and production of TR, however. We set out to examine the relationship between TR and neural responses in primary gustatory cortex (GC) by performing paired recordings of single unit activity and jaw electromyography (EMG) in awake rats presented with strong (0.3 M) and weak (0.03 M) sucrose, and strong (0.001 M) and weak (0.0001 M) quinine, *via* intra-oral cannulae. Comparisons of the time courses of neural and EMG responses revealed that palatability-related signals in GC preceded those in EMG by ~250 ms, suggesting that GC could drive palatability-related orofacial movements. Preliminary analyses further demonstrated that the spiking activity of individual GC neurons was correlated

with the latency of quinine-induced gape bouts. Our results suggest that forebrain activity may influence certain aspects of TR, such as the initiation of palatability-related orofacial movements. Acknowledgements: DC007703

#P81 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Neural dynamics in response to binary taste mixtures

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In natural environments, taste signals an animal encounters typically consist of complex mixtures of tastants. Although a great deal is known about how the taste system processes single tastes presented in isolation, not much is know about how brain integrates different taste signals presented simultaneously. Here we probed single neurons in primary gustatory cortex (GC) for responsiveness to binary taste mixtures. Stimuli consisted of sucrose and citric acid and sucrose and sodium chloride mixed in different ratios (100%/0%, 90%/10%, 70%/30%, 50%/50%, etc.). We tested for three different hypothetical response patterns: 1) Responses varying as a function of sucrose concentration (the monotonic pattern); 2) Responses increasing or decreasing as a function of degree of mixture of the stimulus (the mixture pattern); and 3) Responses that change abruptly from being similar to one pure taste to being similar the other (the categorical pattern). Our results demonstrate the presence of both monotonic and mixture patterns within responses of GC neurons. Specifically, further analysis (that included the presentation of 50 mM sucrose and citric acid) made it clear that mixture suppression reliably precedes a palatability-related pattern, and that the same phenomenon characterizes responses to sucrose/NaCl mixtures. The temporal dynamics of the emergence of the palatability-related pattern parallel the temporal dynamics of the emergence of preference behavior for the same mixtures, as measured by a brief access test. We saw no evidence of categorical coding.

#P82 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Conditioned Taste Aversion Does Not Require Cortical mRNA Synthesis

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Although it has been well established that the gustatory cortex (GC) plays a significant role in the consolidation of taste memory, the precise physiological mechanisms by which this takes place are not fully understood. Notably, taste memory acquisition is traditionally viewed as dependent on cortical protein synthesis (Dudai et al. 2004), but it is unclear whether the learning process requires cortical mRNA transcription. Here, we investigated this possibility using actinomycin D (Act-D), an mRNA synthesis inhibitor that has been shown to impair contextual fear conditioning when infused into the amygdala (Parsons et al 2006). Act-D was microinfused via cannulae implanted into the GC (1.4 mm anterior to Bregma, 5.0 mm lateral, 4.5 mm ventral) of awake rats. Immediately after infusion, a conditioned taste aversion protocol was performed during which the rats were exposed to a taste paired with malaise. Our results indicated that rats form taste aversions even when mRNA synthesis in GC is blocked. These results suggest that memory consolidation is in part independent of mRNA synthesis in the gustatory cortex. It is likely that subcortical production of mRNA, presumably in the amygdala, is sufficient to support cortical protein synthesis and establish taste memory. Acknowledgements: R01 DC-006666/DC/NIDCD NIH HHS/ United States

#P83 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Nutritive value, not taste, is necessary for flavor preferences in mice

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The preference for food is dependent primarily upon the interplay between oral and post-oral factors. The relative contribution of these two systems to food intake is not fully explored. Mice that lack the ability to taste, by genetic deletion of the P2X2/P2X3 purinergic receptor subunits (P2X-KO), can form a preference for monosodium glutamate (MSG) using only post-ingestive cues. The neural mechanisms that underlie this ability remain unknown but likely involve viscerosensory detection of the nutritive qualities of MSG. Thus, the current study assessed if P2X-KO mice can form a preference for the calorie-free sweetener, SC45647 (SC), which, like MSG, is appetitive to WT animals. WT and P2X-KO mice were given training sessions with a flavor alone (e.g. cherry) or with a different flavor (e.g. grape) mixed with 0.05 mM SC. Then all animals were given 2-bottle preference tests with both flavors without SC. During training, WT animals drank more SC than did P2X-KO mice, suggesting that WT, but not P2X-KO mice, can taste SC. However, neither WT nor P2X-KO animals preferred the flavor that was previously paired with SC in flavor alone preference tests. SC-evoked brain activation was measured by expression of the immediate early gene c-Fos (cFLI) in the nuc. solitary tract (nTS)- the primary taste/viscerosensory nucleus. As previously reported for MSG stimulation, SC-induced cFLI in gustatory (rostral) nTS was less in P2X-KO animals compared to WT controls. In viscerosensory (caudal)

nTS, SC-induced cFLI did not differ between WT and P2X-KO mice. Further, within caudal nTS, SC was less effective than MSG in evoking cFLI in both lines. Together, these results suggest that nutritive content, not taste, is necessary to drive food preferences and that this information is represented in the caudal nTS. Acknowledgements: Supported by NIH grants to JMS and Thomas E. Finger (U. of Colorado Denver Medical School, Rocky Mountain Taste and Smell Center, Aurora, CO).

#P84 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Distinct groups of cilia in rat rostral nucleus of the solitary tract (rNST) labeled with ACIII and Arl13b

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All chemosensitive information derived from stimulation of taste receptors in the oro-pharynx relays via the rNST in the brain stem. Neurons of the rNST have been defined using anatomical and histochemical criteria but recently we have also shown that many rNST neurons possess primary cilia, small organelles extending from the cell surface. Primary cilia have been shown to play an important role during development and are involved in cell signaling pathways. The importance of cilia in development is evident in various developmental brain disorders, or ciliopathies, resulting from disrupted cilia function. We studied the location of primary cilia in rNST cells in postnatal rat because they may play a role in signaling during taste processing. A number of markers have been used to identify primary cilia. Two widely used markers are ACIII, part of a cAMP pathway, and Arl13b, part of a cGMP signaling pathway. Previously we reported that ACIII-labeled primary cilia are present in about half of rNST neurons. Somatostatin receptor 3 (SSTR3) and melanin-concentrating hormone receptor 1(Mch1R) co-localize with the ACIII-labeled cilia. Interestingly, though, Arl13b and ACIII-labeled cilia are found on different rNST cells. Neither SSTR3 nor Mch1R co-localizes with Arl13b. In addition, recently we detected a primary cilium in almost every rNST astrocyte using an Arl13b antibody, but not ACIII, further demonstrating differences in rNST primary cilia. Since ACIII couples with a cAMP pathway and Arl13b couples with a cGMP signaling pathway it is possible that the cell types that express different primary cilia play different roles in rNST function. Acknowledgements: NIH NIDCD Grant DC000288

#P85 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Taste responses change over consecutive days in single cells in the rat brainstem recorded in the awake animal

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Theories of taste coding have relied on recordings from single cells in a single session; i.e. snapshots of activity. In contrast, there is evidence that taste responses can change over days (e.g. in chorda tympani fibers, Shimatani et al., Physiol. & Behav., 80(2-3), 309-15, 2003). Here, we present data showing that taste responses in individual cells in the nucleus of the solitary tract (NTS) and parabrachial nucleus of the pons (PbN) vary significantly across consecutive days. Rats were surgically implanted with a chronic microwire assembly into the NTS or PbN, allowed to recover, and water deprived. Rats had free access to a lick spout that delivered taste stimuli or water while cellular activity was recorded. Thus far, in the NTS, 8 animals yielded multi-day recordings (range = 2-5 d; median = 2 d); in the PbN, 5 animals yielded multi-day recordings (range = 2-7 d; median = 2.5 d). To determine whether the recordings on successive days were likely to represent recordings of the same neuron, we examined the similarity of the recorded waveform templates. For 76% of multi-day NTS recordings and 30% of multi-day PbN recordings, waveforms were highly similar (waveform template correlation > 0.99). As a control, this degree of similarity was rare (1.3% of pairs in NTS, <1% of pairs in PbN) when the waveforms were from known-different neurons, recorded on separate microwires. Thus, it is likely most of the recordings across days represent recordings of the same neuron. Analyses of these putative same-cell multi-day recordings showed that responses to individual tastants both appeared and disappeared across days, resulting in shifts in tuning. These data imply that theories of taste coding need to incorporate the dynamic nature of taste response profiles. Acknowledgements: NIDCD R01-DC006914

#P86 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Characterization of Cholinergic Interneuron Populations in the Accessory Olfactory Bulb

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The accessory olfactory bulb (AOB) contains diverse populations of intrinsic interneurons that play a key role in information processing, including choline acetyltransferase (ChAT)-expressing interneurons, which have not previously been identified. We detected these cholinergic interneurons via green fluorescent protein (GFP) signal in $ChAT^{(BAC)}$-eGFP mice, which

allows visualization and quantification of the interneuron cell bodies throughout the bulbar layers of the AOB (Krosnowski et al, 2012). We found significant differences in the number of cholinergic interneurons in the anterior and posterior glomerular layer (GL) and the external plexiform layer (EPL), with the highest numbers of cholinergic interneurons in the anterior GL and posterior EPL. In the posterior EPL, we also noted a high density of GFP+ cells forming a ring around the outer edges of the layer, thus creating a heavy GFP+ population along the border between the anterior and posterior AOB. We then examined the possible role of ChAT interneurons in the AOB using adult male mice exposed to either bedding from a mated pair or to a male aggressor mouse. We monitored the activity marker, c-fos, in these regions and found significantly higher levels of activation of ChAT-expressing cells in the EPL in both exposure groups when compared to activation in control mice, suggesting that this population may serve a role in the processing of social odor cues. Thus, we have identified a significant cholinergic interneuron population in the AOB that varies significantly in the anterior and posterior regions. Thus, our data supports the idea that the anterior and posterior AOB process sensory information differently and suggests that this cholinergic interneuron population may serve to process olfactory information in a region specific manner. Acknowledgements: Supported by research grants NIH/NIDCD 009269, 012831 and ARRA administrative supplement to WL

#P87 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Suppression of Association Synapses in Piriform Cortex During Post-Training Sleep Impairs Odor Memory Selectivity

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Slow wave sleep (SWS) is characterized by slow-wave oscillations in neocortex, as well as sharp waves (SPW) in both the hippocampus and piriform cortex (PCX). Neural activity during SWS is hypothesized to contribute to memory consolidation through "replay" of waking activity patterns. For example, we have demonstrated that imposed replay of odor-evoked activity in the olfactory system during SWS enhances subsequent memory of that odor. Neurons co-activated by an odor are hypothesized to become linked into a cohesive ensemble through strengthening of association synapses. Replay of odor evoked ensemble activity during SWS may help strengthen these connections and improve memory and memory acuity. Here, we tested the hypothesis of that association fiber activity during SWS facilitates replay and memory of recently learned odors by infusing baclofen (or saline) into the PCX during post-training sleep. Baclofen is a GABA-B receptor agonist that has been shown to selectively depress association fiber synapses. Rats were chronically implanted with bilateral cannulae and a recording electrode in the anterior PCX. After recovery, rats were differentially conditioned with CS+ odor/footshock and CS- odor stimuli. During the 4 hours immediately post-training, animals were placed in a sleeping chamber and bilaterally infused with either baclofen or saline. Local field potential and EMG activity were recorded during conditioning, post-training sleep, and test periods. On test day, 24 hours following conditioning, freezing responses to the CS+, CS- and other odors were examined. Preliminary behavioral results suggest that post-training PCX baclofen infusions do not impair memory for the CS+ but reduce odor acuity/enhance generalization of the odor-fear response. Acknowledgements: F31-DC012284 to D.C.B. and R01-DC003906 from the NIDCD to D.A.W.

#P88 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Cholinergic modulation of glomerular odor sensitivity in the olfactory bulb

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In the olfactory system, many studies have shown that cholinergic input to the olfactory bulb is not only involved in learning and memory but also detection and discrimination. In this study we used calcium imaging to explore the cholinergic effect on OB postsynaptic glomerular odor responses. Using mice expressing GCaMP2 in M/T cells, we studied the modulation of dorsal surface glomerular odor concentration-response curves via HDB (horizontal limb of the diagonal band of Broca) stimulation or OB cholinergic pharmacological manipulation. Overall, we find that increased cholinergic OB activation through HDB stimulation or cholinergic-uptake blocker application increases the sensitivity of individual glomerular odor responses by shifting the odor concentration-response curve to the left and decreasing the EC50 by up to one log unit in odor concentration. This effect was observed for all glomeruli tested regardless of baseline odor sensitivity or odorant used. OB application of a muscarinic antagonist completely blocks these shifts, suggesting that the increased sensitivity observed is primarily driven by muscarinic activation. We are now exploring the cholinergic effects on individual OB cell types using two-photon microscopy to further address these effects at the single cell level. Acknowledgements: NIH R03 DC009853 and the Pew Scholars Program in the Biomedical Sciences.

#P89 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

In Vivo Optophysiological Analysis of the Glomerular Unit Response in Mice

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Olfactory bulb glomeruli organize and relay sensory information that arrives from the nose. Odors typically evoke activity across many glomeruli, making it difficult to study their individual role in olfactory processing. To overcome this difficulty we employed transgenic mice in which channelrhodopsin-2 is selectively expressed in genetically identified olfactory sensory neurons; these neurons project their axons to a defined glomerulus and can be activated via pulsed illumination of the olfactory epithelium with a 447nm laser. Through *in vivo* two-photon calcium imaging, we monitored optically evoked neural activity in the glomerulus and nearby juxtaglomerular neurons. Laser pulses reliably activated the glomerulus and evoked calcium responses in juxtaglomerular neuron pools of various sizes. Changing laser pulse width and timing altered the strength, appearance and duration of glomerular and cellular responses. We also identified juxtaglomerular cells that responded to optical activation with decreased intracellular calcium; unlike activated cells, these inhibited cells did not cluster next to the optically activated glomerulus but were spread throughout surrounding areas. We are now investigating how different neuronal responses types relate to the molecular phenotype of the juxtaglomerular cells. To accomplish this we generated hybrid mice, which express GAD67-GFP and/or GAD65-GFP in olfactory bulb interneurons along with the selectively expressed channelrhodopsin-2. In combination, our data provide a uniquely detailed analysis of the neuronal network that comprises a single olfactory glomerulus. Acknowledgements: Supported by NIH grants U24NS057631 and R01DC005259 and by the National Research Foundation of Korea World Class Institute Grant WCI 2009-003.

#P90 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

Top-down modulation of olfactory bulb output by the midbrain serotonergic system.

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The olfactory bulb (OB) receives input from multiple top-down neuromodulatory systems. Serotonergic inputs from the raphe innervate all OB layers and can presynaptically modulate sensory input gain. However, the effects of serotonergic modulation on OB circuitry and output *in vivo* remain unclear. Here, we used Cre-expressing mouse strains to express the calcium indicator GCaMP in periglomerular (PG) cells (using GAD2-cre mice) and in mitral/tufted cells (MTCs) (Cdhr1-cre mice) in order to visualize how raphe stimulation alters resting and sensory-evoked excitation of these two neuron populations. In GAD2-cre mice, brief (1-4 s) electrical stimulation of raphe elicited a slow increase in baseline fluorescence that outlasted stimulation by several seconds, as well as a several-fold increase in the amplitude of inhalation-evoked transients (mean increase, 650 ± 247%). Stimulation of raphe also increased odorant-evoked response amplitudes. Raphe stimulation effects were blocked by the 5-HT2A/C antagonist cinanserin applied locally to the OB. These results suggest that serotonergic inputs to OB transiently increase the baseline excitability of PG cells as well as their responses to sensory input. In contrast, MTCs in Cdhr1-cre mice showed only weak increases in baseline fluorescence upon raphe stimulation onset followed by a more pronounced increase after stimulation offset in some animals. Surprisingly, raphe stimulation did not alter inhalation- or odorant-evoked responses in these neurons. Together, these results demonstrate a differential effect of serotonergic modulation on OB cell types *in vivo* and serve as a starting point for further dissection of the circuit mechanisms underlying the top-down modulation of early olfactory processing as a function of behavioral state. Acknowledgements: Funded by NIDCD DC010915

#P91 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

Neuronal connections from piriform cortex to prefrontal cortical areas of mice

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Piriform cortex, the main olfactory processing area, has been shown to have projections to prefrontal cortex providing olfactory input and receive projections from prefrontal cortex as a potential downstream modulatory pathway. While recent data establish the projections from the prefrontal areas to piriform, the projections from piriform to prefrontal areas remain less understood. To investigate these connections, we utilized retrograde tracing and confocal microscopy. We injected the retrograde tracer, cholera toxin subunit b (CTb),

via iontophoretic injection in the prefrontal areas of lateral orbitofrontal cortex (LO) or agranular insular cortex (AI). The C57BL/6 mice were perfused seven days after CTb injection. The CTb iontophoretic injection created very confined injection sites of a diameter of 150 to 200 µm. Our preliminary data reveal that for mice injected in the LO, CTb positive cells were found in endopiriform nucleus and the ventral-medial area of layer II/III of the anterior piriform cortex. Furthermore, in the LO injected mouse, we found labeled cells in agranular insular and mediodorsal nucleus of thalamus. In the AI injected mice, a similar labeling pattern was seen in endopiriform nucleus with sparsely labeled cells in ventral medial anterior piriform cortex. In both experiments, we found no labeled cells in the dorsal anterior piriform cortex or posterior piriform cortex. Together the data suggest that piriform cortex may be composed of finer anatomical subdivisions that project to prefrontal areas. Whether these subdivisions perform specific functional roles remains to be determined.

#P92 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Neuromodulatory regulation of learning within olfactory bulb

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Intrinsic plasticity within olfactory bulb (OB) circuitry modifies odor generalization gradients based on experience so as to dynamically construct essentially categorical odor representations. This plasticity also is regulated and perhaps gated by neuromodulatory state, and can be manipulated by pharmacological infusions into OB. Cholinergic inputs to the OB acutely regulate the breadth of odor generalization, though the nicotinic component, primarily localized in the glomerular layer, dominates this acute effect. In contrast, muscarinic receptors are predominantly expressed in the external plexiform layer (EPL), which has been increasingly associated with mechanisms of intrinsic learning within OB. We therefore investigated the role that muscarinic modulation of OB circuitry plays in olfactory associative learning. We found that intrabulbar infusion of scopolamine impaired olfactory learning when delivered between training and testing, or when delivered prior to training in studies imposing a similar 45-minute training-testing latency, but not when testing followed training immediately or with a four-minute latency. (Dihydrokainate infusion into OB was used to prevent the retrograde amnestic effect of isoflurane anesthesia). This pattern of results indicates that intact muscarinic responsivity within OB is important for the maintenance of an intact odor memory over this delay period. In contrast, intact alpha-1 noradrenergic responsivity in OB appears permissive for adapting generalization gradients to changes in odor-associated reward levels. Using computational modeling, we are outlining a common framework for OB processing and neuromodulation to understand and explain how OB-based circuitry can instantiate appropriate topologies of learning in response to experience.
Acknowledgements: Supported by NIDCD grant DC009948.

#P93 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

GABAergic gating of olfactory-motor transmission

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Olfactory stimuli induce and modulate locomotor activity during vital behaviors such as homing, predator avoidance, reproduction, foraging and feeding. The neural substrate underlying olfactory-motor behaviors was recently uncovered in sea lampreys (Petromyzon marinus) [Derjean et al. 2010 PLoS Biol 8(12): e1000567]. It consists of a specific neural pathway, extending from the medial part of the olfactory bulb (OB) to the mesencephalic locomotor region (MLR), with a single relay in the posterior tuberculum (PT). In all vertebrates, the MLR acts as a motor command center that controls locomotion via a descending projection to reticulospinal neurons (RS). This oligosynaptic pathway permits movements to be rapidly generated in response to olfactory stimuli, and thus functions as a pathway dedicated to action. The modulatory mechanisms that act on this pathway and that are responsible for affecting the variability of the lamprey's behavioral responses to olfactory inputs are still unknown. We addressed this question by using anatomical (tracers and immunohistochemistry) and physiological (intracellular recordings) techniques. Retrograde axonal tracing from the PT combined with GABA immunofluorescence showed dense GABAergic innervation of the medial OB, a central component of the olfactory-locomotor pathway, suggesting a role for GABA in the modulation of this pathway. Physiological experiments showed that injections of the $GABA_A$ antagonist gabazine (0.1 - 1 mM) into the medial OB considerably amplify or unmask the responses of RS neurons to olfactory inputs. Taken together, our results suggest that GABAergic innervation of the OB acts as a gatekeeper for sensory inputs to motor control centers.
Acknowledgements: Great Lakes Fishery Commission CIHR NSERC FRSQ

#P94 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

Distinct roles of bulbar muscarinic and nicotinic receptors in olfactory discrimination learning

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The olfactory bulb (OB) and piriform cortex (PC) receive dense cholinergic projections from the diagonal band of Broca in the basal forebrain. Cholinergic modulation within the PC has long been proposed to serve an important function in olfactory learning and memory. We here investigate how olfactory discrimination learning is regulated by cholinergic modulation of the OB inputs to the PC. Using pharmacological manipulation of the OB, we examined the role of bulbar cholinergic signaling in rats' performance on a two-alternative choice odor discrimination task. Results show that blocking bulbar cholinergic signaling significantly slows learning, although the relative contribution of muscarinic (MAChRs) and nicotinic receptors (NAChRs) depends on task difficulty. Specifically, blocking MAChRs (38 mM scopolamine) impaired learning for nearly all odor sets tested (n=13), whereas blocking NAChRs (19 mM MLA) only affected learning when the task was made difficult by using perceptually similar odors. This pattern of behavioral effects is consistent with predictions from a recently developed model of cholinergic modulation in the OB and PC (de Almeida et al., 2012). The model suggests that MAChRs and NAChRs serve complementary roles in regulating OB output and cortical learning. Namely, NAChRs determine the output *rate* within each OB channel and therefore regulate the overlap between learned representations in the cortical network. On the other hand, MAChRs control the *timing* of spikes across OB output channels and, as a consequence, regulate the strength of odor representations in the cortical network. Together, these results suggest that MAChRs in the OB serve a general role in regulating learning, whereas NAChRs are only critical when there is substantial overlap in the sensory inputs.
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#P95 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

Retronasal odor intensity coding in the dorsal olfactory bulb of rats

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In nature food contains many volatile chemicals with a wide range of concentrations. The volatiles, when released in the mouth while eating, travel to the nasal cavity via the nasopharynx evoking a retronasal smell which contributes to food flavor. The olfactory system is responsible for encoding not only the quality but also the concentration of the volatiles present in food. It is believed that each odor is represented by a unique glomerular activation pattern in the olfactory bulb. However, whether and how retronasal odor concentration is encoded by the spatiotemporal activity pattern of olfactory glomeruli, without confounding the quality of a different odorant, remains unknown. In this study we optically imaged the retronasal odor-induced calcium responses of olfactory receptor neurons in the dorsal olfactory bulb in double-tracheotomized rats. We found reliable concentration-response curves that differed between odors. MDS of the spatial OB patterns suggest that ambiguity among select stimuli may occur. Further, the relation between dynamics and concentration differed remarkably among retronasal odorants. Understanding of coding for retronasal odor intensity has potentially important implications in the feeding behavior and flavor neuroscience.

#P96 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

Intrinsic oscillatory discharge patterns in mitral cells of the mouse accessory olfactory bulb

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The accessory olfactory bulb (AOB) represents the first stage of central information processing in the rodent accessory olfactory system. In the vomeronasal organ, social chemosignals activate sensory neurons which form synaptic contacts with mitral/tufted cells, the main excitatory projection neurons in AOB. Bypassing the thalamo-cortical axis, these neurons project directly to higher brain regions such as amygdala and hypothalamus. Despite their physiological significance, the intrinsic properties of mitral cells and their role in social information coding and signal integration in the AOB are not fully understood. Here, we investigate the biophysical properties of AOB mitral cells using both voltage- and current-clamp whole cell recordings from optically identified neurons in acute mouse AOB tissue slices. We identify a population of mitral cells that display slow oscillatory discharge patterns which persist after

pharmacological inhibition of synaptic transmission (AP5, NBQX and gabazine), revealing the network-independent origin of this bursting behavior. The underlying subthreshold membrane potential fluctuations with alternating up/down states display a high degree of periodicity. Using electrophysiological and pharmacological approaches, we analyze the basic ionic mechanisms underlying mitral cell oscillatory discharge. Our data demonstrate a complex interplay of multiple voltage-gated ionic conductances, such as TTX-sensitive sodium channels and TEA-sensitive potassium channels as well as conductances dependent on both intra and extracellular calcium, which maintains rhythmicity. The oscillatory discharge patterns observed in AOB mitral cells could play an important role in the signal coding and / or hormonal homeostasis controlled by mitral cells target regions in higher brain centers.

#P97 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Lateralized differences in olfactory bulb volume relate to lateralized differences in olfactory function

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The present study aimed to investigate whether side differences in olfactory bulb (OB) volume correlate to respective differences in olfactory function. In a total of 164 healthy volunteers volumetric measures of the OBs were performed plus lateralized measurements of odor thresholds and odor discrimination. Side differences were defined as 10% difference between the left and right OB. In 39 cases volumes on the right side were larger than on the left side, whereas in 29 cases it was the other way around. Subjects with larger right-sided OB volumes were found to be more sensitive to odorous stimulation of the right as compared to the left nostril in terms of odor thresholds and odor detection; while correspondingly, higher sensitivity of left nostrils was observed in individuals with larger OB volumes on the left side. These data appear to suggest that OB volume is partly dependent on lateralized influences on the olfactory system, reflecting its lateralized organization. Acknowledgements: Supported by a grant from the "Roland Ernst Stiftung" to TH.

#P98 **PPOSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Olfactory Sensory Neuron Physiology and Exposure-Induced Plasticity Are Altered in Adult Olfactory Marker Protein Knockout Mice

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Olfactory marker protein (OMP) is highly and selectively expressed in olfactory sensory neurons (OSNs) across species, but its function remains elusive. Previous *in vitro* studies of MOR23-expressing OSNs suggested that OMP accelerates the OSNs' response to odorants and may modulate the odorant-selectivity of OSNs (Lee et al. 2011 *J Neurosci 31:2974-82)*. Here we performed *in vivo* optical imaging in adult mice expressing the fluorescent exocytosis indicator synaptopHluorin from the OMP locus. We compared the spatiotemporal patterns of odor-evoked transmitter release from OSNs in mice that were heterozygous for OMP (OMP-/+) or OMP-null (OMP-/-) and found that these patterns developed on a slower timescale in OMP-/- mice but eventually reached the same magnitude as in OMP-/+ mice. In OMP-/- mice, OSNs innervating a given glomerulus also responded to a broader range of odorants than in OMP-/+ mice. These results extend the previous *in vitro* findings in MOR23-expressing OSNs to other OSN populations *in vivo*. We next evaluated the effects of a 7 day odor exposure paradigm on these spatiotemporal patterns in adult OMP-/+ and OMP-/- mice. We found that in OMP-/+ mice, odorant exposure reduced the number of glomeruli receiving OSN input evoked by the exposure odorant and the magnitude of those inputs but had no effect on the response to unrelated odorants. In contrast, in OMP-/- mice this experience-dependent suppression was observed in the responses to all test odorants, not just the exposure odorant. These results suggest that OMP not only conveys odor-selectivity on OSNs but also plays a role in restricting experience-dependent plasticity to specific OSN populations. Acknowledgements: This work was supported by the National Institute on Deafness and Other Communication Disorders (R00 DC009442 to JPM).

#P99 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Floral Preference is reflected in the Neuroanatomy of the Olfactory System in Mason Bees (*Osmia*)

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Locating food sources is important for all insects, and in many species the olfactory system is crucial for finding suitable sources. Two main strategies can be found: either to be able to use many different food sources (generalists) or to be specialized on a single or only few food sources (specialists). In bees, both

generalist and specialized species can be found that collect pollen and nectar either from many plant families (polylectic) or from only few species (oligolectic). In some cases, both types of food preferences can be found within the same genus, like in the mason bee genus *Osmia*. Here we investigate how the floral preference is reflected in the neuroanatomy of the olfactory system. We employed confocal microscopy scanning and 3D-reconstruction for quantitative analyses of major neuropile volumes. We counted the number of functional units (glomeruli) within the antennal lobe, the first olfactory neuropile in insects, and quantified synaptic structures in higher-order sensory integration centers (mushroom bodies). The investigated *Osmia* species showed significant differences in selected neuropile volumes and also a large interspecies variance in glomerular numbers, correlated to floral preference. The strictly oligolectic species *Osmia adunca* showed the smallest number of glomeruli, whereas all polylectic species showed larger glomerular numbers. The mushroom bodies of polylectic and oligolectic species showed the same density of synaptic structures, but expressed significant volume differences in the subregions that process olfactory information. Chemical analyzes of host-plant odors and behavioral tests will be next steps to understand the large impact of floral preference on the complexity of the olfactory system in bees. Acknowledgements: DFG KE-1701 1/1

#P100 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Temporal-spatial transformation in the piriform cortex

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Mitral cells of the olfactory bulb respond to stimuli with brief and temporally precise transient changes in the firing rate (sharp events) that tile the inhalation cycle. This suggests that information about odorants can be encoded by the temporal sequence of these events. Here we propose a class of computational models for the olfactory cortex that can detect such sequences and convert them into a spatial pattern that can be recognized by standard attractor networks. We propose that the olfactory cortex contains groups of cells that can be sequentially activated by inputs from mitral cells synchronized at different phases of the respiratory cycle. Neurons in each group can be persistently activated by virtue of, for example, an intrinsic bistability mechanism. The pattern of activation of neurons in each group carries a snapshot of coincidences in mitral cell sharp events at a particular phase of the breathing cycle. Due to long-range intracortical connectivity, the activation of one group "enables" bistability in another group which can then form a snapshot of mitral cell activity at a later phase of the respiratory cycle. In this way, persistent activation of groups of neuron occurs sequentially, each in turn representing the olfactory bulb activity at a certain phase of the sequence. We further show that sharp events in mitral cell responses occur at a preferred phase of gamma cycles (measured in the field potential). Given that there are only a few gamma cycles within a sniff, the number of groups needed to define gamma cycle specific snapshots of an odorant is not large. Recognition may occur when the spatial pattern becomes sufficient to distinguish among the potential odorants.

#P101 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Unique Cholinergic Interneuron Populations in the Mouse Accessory Olfactory Bulb: Neurochemical Expression and Fiber Density

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The accessory olfactory bulb (AOB) is a primary central processing site of sensory information detected via the vomeronasal organ. The AOB contains diverse populations of intrinsic interneurons. We detected a largely unidentified choline acetyltransferase-expressing (ChAT) cholinergic interneuron population using ChAT$^{(BAC)}$-eGFP mice. Here we classified their neurochemical expression and distribution throughout the AOB. We then determined if this cholinergic interneuron population differs from other known populations of interneurons in the AOB and main olfactory bulb (MOB). Similar to the MOB (Krosnowski et al 2012), we found that all cholinergic interneurons are neither dopaminergic nor GABAergic. While most ChAT expressing cells in the external plexiform layer (EPL) of the AOB are not glutamatergic, we found some coexpression between ChAT-GFP and GluR2/3, a glutamatergic marker, in contrast with results obtained from the MOB. Also, unlike the cholinergic interneuron population in the MOB, the majority of cholinergic interneurons in the AOB do not express a calcium binding protein, calbindin-D28K. Further, clear differences can be seen between cholinergic nerve fibers in the internal plexiform layer (IPL) of the MOB and the AOB. Unlike in the MOB, where the highest density of cholinergic nerve fibers was found in the IPL, in the AOB, the IPL contains the fewest visible fibers. Instead, the majority of cholinergic fibers in the AOB are found in the EPL. Thus, our data supports the idea that the intrinsic cholinergic interneuron populations in the AOB are distinct from previously identified interneuron populations in both the MOB and AOB and this suggests that they play a unique role in signal processing in the accessory olfactory system. Acknowledgements: NIH/NIDCD 009269, 012831 and ARRA administrative supplement to WL

#P102 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Blend Processing by Protocerebral Neurons of *Manduca sexta*

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The male moths of *Manduca sexta* are more attracted to a mimic of its natural female sex pheromones, composing of only two essential components in a ratio that is found in its natural pheromones. Deviation from this ratio causes reduced behavior. The projection neurons innervating the pheromone responsive region of the male antennal lobe produce maximal synchronized spiking activity in response to blends consisting of the two components centering around the natural ratio, leading to a hypothesis that blend ratios are encoded in neuronal synchrony. To test this hypothesis, we investigated the physiological and morphological features of down-stream protocerebral neurons that were challenged with stimulation of single pheromone components and their blend of different ratios. We found a small proportion of protocerebral neurons showing stronger responses to the blend of natural ratio whereas many other neurons did not distinguish these blends at all. In a multi-dimensional analysis, we also found the population response mapped onto the second principle axis displayed most distinction among the two pheromone components and their blend, and the distinction occurred prior to the peak population response - a result consistent with an earlier observation where neural synchrony in the antennal lobe tends to maximize before the firing rate reaches its peak. Moreover, the response patterns of protocerebral neurons are very diverse, indicating the complexity of internal representation of odor stimuli at the level of protocerebrum. Acknowledgements: This work was supported by NSF grant DMS-1200004 to HL, NIH grant R01-DC-02751 to JGH

#P103 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Comparison of changes in odor-induced firing of mitral cells and oscillations in the local field potentials in mice learning to discriminate odors

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Odor induced mitral cell firing and changes in local field potentials (LFPs) are modified as an animal learns to discriminate between odors. In previous work we reported that as the animal learns to discriminate between odors in go-no go odor discrimination tasks synchronized unit firing of mitral cells develop divergent responses to rewarded and unrewarded odors, and convey important information on odor quality in addition to odor identity in awake behaving mice (Doucette et. al. Neuron *69,* 1176–1187, 2011). LFPs reflect integrated signals from cell ensembles also show divergent responses. However, how mitral cell firing and local LFPs are related and more importantly how these are related on a trial-by-trial basis when the animal makes mistakes remains to be elucidated. Here our preliminary data indicate that unit firing and beta oscillations of LFPs (10-35 Hz) show related changes during the learning process of the go-no go task: at the beginning of the task, there is no or very weak divergent odor responses for both signals, while obvious and strong divergent responses are found as the mice learn to discriminate the odor pairs. Acknowledgements: DC00566 and DC04657

#P104 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Identification of Microglia in the Peripheral Deafferentation Response of the Adult Zebrafish Olfactory Bulb

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Our lab has been examining the potential role of microglia in the deafferentation response of the zebrafish olfactory bulb. We previously used phagocytosis-dependent labeling with DiA to illustrate the putative microglial response following olfactory organ ablation. DiA-labeled puncta in the deafferented olfactory bulb increased dramatically in number and then diminished over the course of a week. The labeling pattern corresponded directly to areas of the bulb with damaged axons. In that study, we were unable to identify the labeled profiles conclusively as microglia. The current study seeks to confirm both the presence and active role of microglia in the deafferented zebrafish olfactory bulb using an antibody to zebrafish microglia (anti-4C4). Zebrafish were treated either with cautery ablation or Triton X-100 application to the olfactory organ to cause either permanent or temporary deafferentation of the bulb. We hypothesized that the pattern of anti-4C4 labeling would mimic the pattern seen with DiA. We found that the olfactory bulb had an obvious increase in 4C4-positive microglia 1 day following both permanent and temporary treatments. These 4C4-positive profiles had primarily amoeboid morphology; they were found throughout the bulb layers but were concentrated around the degenerating axons. Over the next several days, the 4C4-positive microglia appeared to decrease in number; they also changed to mostly ramified morphologies. This pattern overlaps with the DiA results but also appears to show additional microglia not actively phagocytizing axonal debris. Thus, there is a profound microglial response immediately after both permanent and temporary deafferentation in the adult zebrafish olfactory bulb that sharply declines over the next several days. Acknowledgements: Supported by NIH-NIDCD #011137 (CBJ)

#P105 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Influences of lateral amygdala activation on piriform cortical odor processing

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Olfactory sensory processing in the piriform cortex requires the synergy of odorant ligand input, local inhibitory feedback loops, and interregional modulation, in order to synthesize emotionally relevant and contextually significant odor percepts. Reciprocal connectivity between the piriform cortex and higher processing regions, such as the lateral entorhinal cortex and amygdala, provide currently understudied routes through which odor processing in the piriform may be regulated. We have employed optogenetic techniques to investigate how activation of lateral amygdala (LA) during odor presentation affects piriform cortical odor processing. We have performed single unit recordings of both spontaneous and odor-evoked activity in the anterior piriform cortex, and summarized a range of LA-influenced changes in piriform activity. We have also begun using a fear conditioning model to investigate the influences of emotional significance on odor processing in the piriform. We aim to describe how such contextual changes affect the precision of both cortical odor processing and behavioral odor perception.
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#P106 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Wild Scents: comparing the olfactory anatomy of caged and wild mice

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We have previously detailed the subtle neuroanatomical changes we found in the glomeruli of olfactory bulbs from genetically identical mice reared in cages with different levels of ventilation (Oliva and Salcedo et al, 2010). In these mice, we were able to correlate these glomerular changes with marked increases in aggressive behavior towards invader mice, highlighting the exquisite sensitivity a mouse's olfactory neuroanatomy has to its environment. In order to examine the broader effects that environment may have on the formation of the olfactory system, we have trapped wild house mice from the Denver environs and have rigorously characterized the neuroanatomy of their main olfactory bulbs (MOB) using MATLAB mapping software developed in-house and immunohistochemical techniques. On gross examination, the MOBs from the wild mice do not appear to be significantly different from their caged brethren. Nor did we find any significant immunostaining differences in OMP of GAP43 labeling of the MOB. Although somewhat smaller, the wild olfactory bulbs had an estimated number of glomeruli (using Meisami's Correction) that does not differ significantly from the estimated number of glomeruli found in the MOBs of their caged counterparts. Curiously, we do find a dramatic difference in the distribution of olfactory sensory innervation across the surface of the MOB: caged mice tended to have larger glomeruli that occupied a significantly larger portion of the glomerular layer then did the wild mice. This distribution was particularly pronounced in the ventro-medial portion of the bulb around the AOB. These results provide further evidence that olfactory environment plays a role in fine-tuning the formation and maintenance of glomeruli in the main olfactory bulb.
Acknowledgements: NIDCD

#P107 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Assessment of nasally administered insulin-like growth factor-I accumulation in the cerebrum of mice with resected olfactory bulb

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Objectives: To show the role of the olfactory bulb in the delivery of nasally administered insulin-like growth factor-I (IGF-I) to the brain *in vivo*. Nasal administration of IGF-I has been shown to enable drug delivery to the brain beyond the blood brain barrier *in vivo*. IGF-I is associated with the development and growth of the central nerve. **Methods:** The ratio of uptake of nasally administered ^{125}I-IGF-I in the cerebrum to uptake in the blood of male ICR mice with resected left olfactory bulb (8 weeks of age, the model mice) was compared to that of the sham-operated male ICR mice (8 weeks of age, the control mice). We exposed and resected the left olfactory bulb, cutting the frontal bones of model mice, and just exposed the left olfactory bulb in control mice under anesthesia. ^{125}I-IGF-I (human, recombinant) saline solution was obtained from PerkinElmer Japan (Yokohama, Japan), and 10μl was instilled into the left nostril of each mouse with a microinjection pipette under anesthesia. The radioactivity of the samples was measured with gamma spectrometry. The accumulation of the nasally administered neuronal tracer (fluoro-ruby; dextran tetramethylrhodamine) in the epithelium of mice was assessed in frozen sections under a fluoroscopic microscope. **Results:** The ratio of uptake of nasally administered ^{125}I-IGF-I in the cerebrum to uptake in the blood of the model group was significantly decreased compared to the control group. The accumulation of nasally administered neuronal tracer in the nasal epithelium of mice was significantly prevented by the resection of the olfactory bulb. **Conclusions:** Olfactory bulb resection results in the reduced delivery of nasally administered IGF-I to the brain due to the disconnection of the olfactory nerve between the nasal epithelium and olfactory bulb *in vivo*.
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#P108 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

Dynamics of reward-mediated neural plasticity in honey bee antennal lobe glomerulus

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Recent studies of neural plasticity in the honey bee antennal lobe (AL) show the response dynamics of uniglomerular projection neurons (uPNs) to an odor change after association of that odor with sucrose reinforcement. The octopamine (OA), released by the ventral unpaired median neuron (VUM), is necessary for these neural plasticity changes. Using anti-OA staining, we found that the varicosity-like distributions of VUM branch mostly in the cortex of the glomerulus, where it potentially modulates olfactory receptor neurons (ORNs), local interneurons (LNs) and uPNs. We develop a biophysical model of the AL circuit to investigate modulatory mechanisms that can explain existing data on the dynamical changes of uPNs during associative learning, and lead to insights for new experiments. First, we hypothesize that OA release from VUM varicosities would be dependent on correlated firing between ORNs and VUM during associative learning. This mechanism implies simultaneous cholinergic and octopaminergic transmission to PNs. Second, OA release from VUM acts on AmOA1 receptors expressed in LNs. AmOA1 activation increases the excitability of LNs, leading to increased inhibition of PNs. Third, release of OA leads to direct activation of beta-adrenergic-like OA receptors. This increases the levels of cAMP, triggering PKA-dependent translation and upregulation of alpha7 nicotinic acetylcholine receptor (nAChR) subtypes. nAChR-dependent Ca2+ influx triggers transcription factors that upregulate transient Shal-type K+ channels, preventing excessive membrane depolarization. Based on these hypotheses, we propose the model to characterize dynamics of the uPN as a function of the relative expression of Shal-type K+ channels and OA release. Acknowledgements: NIH-NCRR RR014166 and NIH grant R01 DC011422

#P109 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

In vivo imaging of odor-evoked responses in the mouse olfactory bulb using the FP voltage sensor ArcLight and the calcium sensor GCaMP3

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Optogenetic reporters of membrane potential allow for recording of genetically distinct populations of neurons, although their usefulness to date has been limited by poor in vivo expression, small signal sizes and slow kinetics. The fluorescent protein (FP) voltage sensor ArcLight exhibits a change in fluorescence to a 100 mV depolarization five times larger than previously reported probes in HEK 293 cells. However, recordings of ArcLight in mammalian neurons have been limited to cultured neurons. The goal of the present study was to examine ArcLight responses in the olfactory bulb in an *in vivo* preparation, and compare them to those of the genetically encoded calcium indicator GCaMP3. AAV-1 viral transduction was used to express ArcLight and GCaMP3 in the mouse olfactory bulb. Odors were presented at different stimulus duration and concentrations, and the resulting patterns of activation were imaged. Odor-specific patterns of activation were obtained from both ArcLight and GCaMP3, although only ArcLight had sufficiently fast temporal kinetics to clearly detect population activity elicited by individual sniffs to an odor. The results indicate that ArcLight can be used as a reliable detector of odor-evoked population signals in the mouse olfactory bulb. Acknowledgements: Supported by US NIH Grants DC005259 and NS057631, Grant WCI 2009-003 from the National Research Foundation of Korea, and an James Hudson Brown – Alexander Brown Coxe Fellowship from Yale University.

#P110 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

Expression and Activity of Glucagon-like Peptide-1 in the Mouse Olfactory Bulb

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A number of peptides and hormones that are known to regulate energy metabolism or feeding behavior have been identified in the olfactory system. These hormones are thought to modulate olfactory perception and function to suppress or promote

appetite. Glucagon-like peptide-1 (GLP-1) is an incretin peptide that also suppresses food intake, and *in situ* hybridization in rat has suggested that both GLP-1 and its receptor are present in the olfactory bulb (OB). Furthermore, GLP-1 modulation of taste sensitivity has been reported for taste buds, prompting us to speculate a similar role in the olfactory system. Using transgenic mice expressing YFP under the preproglucagon (PPG) promoter, we confirm that a population of YFP-immunoreactive neurons exists in the granule cell layer (GCL) of the OB, indicative of GLP-1 producing cells. The labeled neurons had a typical granule cell morphology with a single axon projecting into the adjacent mitral cell layer (MCL). We observed strong immunoreactivity for the GLP-1 receptor in the MCL and in sparse cells in the GCL in olfactory marker protein (OMP-GFP) transgenic mice. Binding of biotinylated GLP-1 to the GLP-1 receptor was visualized within the same regions. We confirmed the presence of functional GLP-1 receptors on mitral cells (MCs) using whole-cell patch-clamp recordings in acute OB slices. Bath perfusion of 1 μM GLP-1 or its stable analogue, exendin-4, resulted in a significant increase in the evoked action potential frequency (370% for GLP-1 and 170% for exendin-4) and a concomitant decrease in the interburst interval in about 60% of the sampled MCs. These results show that GLP-1 is synthesized locally in the OB and directly affects the firing properties of MCs, suggesting a potential paracrine modulation of olfactory output with satiety. Acknowledgements: This work was supported by R01 DC003387 from the NIH/NIDCD, a Creative Research Council (CRC) award from FSU, a Project Grant 1025031 from NHMRC Australia, and MR/J013293/1 from the MRC United Kingdom.

#P111 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Enhanced Survival of Newly Formed Cells Contributes to Restoration of Olfactory Bulb Volume Following Reversible Deafferentation in Adult Zebrafish

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Our lab has shown that chronic partial deafferentation, achieved through unilateral chemical ablation of the olfactory epithelium with Triton X-100, results in a decrease in olfactory bulb volume, while cessation of treatment allows bulb volume to recover. We hypothesized that alterations in cell genesis and/or survival would be involved in restoration of olfactory bulb size. Bromodeoxyuridine (BrdU) administration was used to examine newly formed cells in the brain of adult zebrafish, with short-term survival allowing investigation of patterns of cell proliferation and long-term survival allowing examination of cell survival and fate. We first compared two methods of BrdU administration: immersion of fish in the drug versus intraperitoneal injection. While both methods revealed similar numbers of newly formed cells, injection of the drug resulted in loss of fewer fish during treatment. Next, we examined potential alterations in cell genesis and/or cell survival resulting from reversible partial deafferentation. Repeated detergent treatment followed by BrdU exposure showed no difference in the number of dividing cells in the olfactory bulb, indicating that cell genesis is not affected. There was, however, an increase in newly formed cells that survived when the detergent treatment ceased, indicating that cell survival contributes to the restoration of bulb volume during the period of reinnervation. When fish were exposed to BrdU before the repeated detergent treatment, there appeared to be no effect on the number of newly formed cells. Thus, enhanced cell survival, rather than cell genesis, appears to be a contributing factor in the restoration of olfactory bulb volume following return of innervation in a reversible deafferentation model. Acknowledgements: Supported by NIH-NIDCD #011137 (CBJ)

#P112 **POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS**

Characterizing Olfactory Bulb Circuitry using Intrinsic Flavoprotein Fluorescence Imaging

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The main olfactory system has distinct subsystems that differ in the chemosensory stimuli to which they respond and the connections they make to the brain. In contrast to the canonical glomeruli of the main olfactory bulb (MOB), individual necklace glomeruli (NGs) receive heterogeneous olfactory sensory neuron (OSN) innervation [including semiochemical-sensitive OSNs expressing guanylyl cyclase D (GC-D)] and display extensive intrabulbar connections. This organization suggests that NGs integrate multiple olfactory signals. To better understand the functional circuitry associated with NGs, we examine the trans-synaptic spread of neuronal activity using intrinsic flavoprotein fluorescence (FF) imaging. FF imaging measures the changes in endogenous fluorescence produced by mitochondrial flavoproteins that accompany increased metabolic demand. The FF signals correspond to neuronal activity and can be followed across synapses, thus facilitating the mapping of functional circuits. Studies in horizontal MOB slices from 3-5 w.o. mice exhibit robust FF signal spread from the glomerular layer (GL) to the external plexiform layer (EPL) following electrical stimulation (1-4 s, 10-50 Hz, 10-100 μA) of individual canonical and necklace glomeruli. Bath application of 10 mM gabazine increased lateral stimulus-dependent FF signal spread in the GL/EPL, and resulted in a 2-fold increase in FF signal amplitude in the EPL. Single NG stimulation (from mice expressing green fluorescent protein under control of the gene encoding GC-D) results in reduced FF signal amplitude but prolonged FA signal duration compared to canonical glomeruli. The use of FF imaging should help reveal basic strategies of information processing in the MOB and its subsystems. Acknowledgements: NIDCD (DC005633), NIGMS (GM008181), NINDS (NS063391)

#P113 POSTER SESSION II: OLFACTION DEVELOPMENT; TASTE CNS; NEUROIMAGING; OLFACTION CNS

DIFFERENTIAL MODIFICATIONS OF SYNAPTIC WEIGHTS DURING ODOR RULE LEARNING: DYNAMICS OF INTERACTION BETWEEN THE PIRIFORM CORTEX WITH LOWER AND HIGHER BRAIN AREAS

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Learning of a particularly difficult olfactory-discrimination (OD) task results in acquisition of rule-learning, a process that requires prolonged and extensive training. Previously, we demonstrated enhanced synaptic connectivity between the piriform cortex (PC) and its ascending and descending inputs from the olfactory bulb (OB) and orbitofrontal cortex (OFC) following OD rule learning. Here, using recordings of evoked field post-synaptic potentials in behaving animals, we examined the dynamics by which synaptic connectivity from the OB and OFC to the PC are modified during rule acquisition. We show profound differences in the dynamics and strength of synaptic connectivity modulation between the ascending and descending inputs. During rule learning acquisition, the ascending synaptic connectivity from the OB to the anterior and posterior PC is simultaneously enhanced. Notably, the daily OB electrical stimulation used to examine the strength of synaptic inputs enhanced the rate of rule learning. In sharp contrast, the synaptic input in the descending pathway from the OFC was significantly reduced during rule learning acquisition. OFC stimulation had no effect on the rate at which the rule was acquired. Once rule learning was established, the strength of synaptic connectivity in the two pathways resumed its pre-training values. We suggest that acquisition of olfactory rule learning requires a transient enhancement of ascending inputs to the PC, synchronized with a parallel decrease in the descending inputs. This combined short-lived modulation is required to enable the PC network to reorganize in a manner that enables it to first acquire and then maintain the rule.

#P114 POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY

Human exposure to acrolein – time dependence on TRPA1 agonists

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The objective of the study was to examine the time dependence on sensory irritation potency of acrolein (2-propenal) in humans. Concentrations at or below earlier reported thresholds that initially are too low to evoke sensory irritation in the eye but might do so in exposures up to 60 minutes were used. Acrolein is a known TRPA1 agonist present in cigarette smoke, smoke from fires, automobile exhaust and smog. The TRPA1 channel is activated by electrophilic compounds that form covalent bonds with cysteine residues. Because of this mechanism of activation one can expect duration of exposure to be of importance in evoking sensory irritation. The exposures occurred in an exposure chamber and the subjects were breathing fresh air through a mask that covered the nose and mouth. All participants took part in four exposure conditions, differing in duration and concentration. The concentrations of acrolein (diluted in heptane) were 0.35, 0.07, 0.05 and 0 ppm (during 15, 45, 60 and 30 min, respectively). During the 30 minutes of exposure subjects were exposed to only heptane at the same concentration as in the other exposures (4.9 ppm). During exposure, eye irritation was rated on Borg's CR-100 scale. Human exposure to acrolein at sub-threshold concentrations showed a cumulative effect on sensory irritation. During exposure to 0.35 ppm (but not 0.07 and 0.05 ppm) acrolein evoked a significant increase in irritation compared to the control condition after about 12 minutes of exposure. During exposure to 0.07 and 0.05 ppm only some of the subjects reported increased irritation after about 30 minutes of exposure. A large variability in reported sensory irritation was seen between individuals and this may be due to individual differences in the ability to remove the electrophilic irritants from the cornea.
Acknowledgements: The Swedish Research Council FORMAS

#P115 POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY

Solitary Chemosensory Cells in Human Nasal Epithelium

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Solitary chemosensory cells (SCCs) described in rodents rely on the bitter taste transduction cascade to detect potential irritants within the airways. SCCs express all of the taste GPCR signaling effectors including T2R bitter taste receptors, α-gustducin, PLCβ2, and the transduction channel TRPM5. SCCs are

innervated by the trigeminal nerve and when stimulated evoke protective airway reflexes such as sneezing, apnea and local inflammation (Tizzano et al., 2010; AChemS 2012). We have begun investigating SCCs in human sinonasal epithelium and their clinical implications. Previously we and others reported that cells resembling SCCs occur in human biopsy material near the vestige of the vomeronasal organ (Braun et al., 2011) as well as within the turbinates (Barham et al 2013; AChemS 2012). However, the exact distribution and abundance of SCCs in humans is unknown. To map the distribution of SCCs, we obtained middle and inferior turbinate mucosa from human patients that were free of sinonasal disease, but were undergoing surgical procedures requiring removal of this tissue. Whole mount tissue was stained with antibodies against TRPM5 and villin, which is expressed at the apex of microvillous, but not ciliated, epithelial cells. TRPM5-immunoreactive cells were scattered heterogeneously in the sinonasal tissue. The cells were most abundant on the ridges of the turbinates and less abundant on the lateral margins. Many TRPM5 immunoreactive cells also labeled with the villin antibody, suggesting that TRPM5 is present in microvillous but not ciliated cells of the epithelium. Studies are in progress to determine if disease state alters the distribution or abundance of these cells and whether SCCs in humans are innervated by the trigeminal nerve, as in rodents. Acknowledgements: R01 DC009820 (TEF and SCK) P30 DC04657 (to D. Restrepo)

#P116 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Responses to change in oral temperature by neurons in the mouse medullary dorsal horn and nucleus of the solitary tract

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Psychophysical data show the temperature of sapid solutions influences flavor. However, it is not entirely clear how central neural circuits for oral sensation encode temperature input. The trigeminal subnucleus caudalis (Vc) is a brainstem somatic relay receiving temperature signals from the oro-facial region and implicated for oral thermosensation. Additionally, the solitary tract nucleus (NTS), the first central taste relay, also receives thermal input from the mouth. Here we compared neural responses of NTS and Vc to intraoral thermal stimulation in anesthetized mice to assess the contribution of activity in these structures to oral temperature responses in brain stem. Extracellular single-unit activities of NTS thermo-gustatory neurons and Vc thermo-somatic cells were recorded after application of different temperature stimuli to tongue, including cold (5 and 10 °C), cool/ambient (17 and 23 °C), and warm/hot (30, 45, and 48 °C). Temperature stimulation was achieved rapidly by oral flow of thermally varied water. Seventy-two neurons were obtained; 34 from Vc and 38 from NTS. Analyses revealed significant differences between NTS and Vc in responses to thermal stimuli [$F(1, 70) = 5.80$, $P<0.05$], and a significant interaction between nucleus and temperature [$F(7, 490) = 61.34$, $P<0.001$]. Cold stimuli produced a marked excitation in the majority of Vc cells (30/34). In the Vc, mean firing rates decreased sharply from 109.9 to -49.2 Hz with oral warming. In NTS, 76% of cells (29/38) were influenced by temperature; 9 were excited by cold, 15 excited by warmth, and 5 responded to both kinds of stimuli. Thus, excitation to oral warming was more prevalent in NTS. Results suggest Vc and NTS process oral temperature information in distinct manners. Acknowledgements: NIH DC 011579 (CHL)

#P117 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Cholinergic Regulation by ChAT and TrpM5 – Expressing Microvillous Cells in Main Olfactory Epithelium and Solitary Chemosensory Cells in Nasal Cavity and Upper Airway

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Chemosensory detection of inhaled irritating, harmful substances in the nasal cavity and upper airway is essential for vital organ protection. Previously, we identified a population of micorvillous cells (MCs) in the main olfactory epithelium (MOE) that expresses both transient receptor potential channel M5 (trpM5) and choline acetyltransferase (ChAT). Despite their distinct morphology and distribution, the MCs share properties, such as cell marker expression and chemosensibility with solitary chemosensory cells (SCCs) found in the nasal respiratory epithelium, vomeronasal duct and trachea (Lin et al. 2008, Ogura et al. 2010, 2011). Here, we provide comparative studies of MCs and SCCs at different regions. Using single cell Ca^{2+} imaging, we compared intracellular Ca^{2+} response profile to chemical stimuli. We found that the order of responding cell percentage to various stimuli was similar among these cells (high concentration odorants > denatonium > ATP > acetylcholine (ACh)). Because of the low percentage of ACh-sensitive MCs and SCCs, ACh released from these cells may play a role in paracrine regulation to influence neighboring cells. Using Ca^{2+} imaging on intact epithelial preparations, we found that ACh-induced increases in intracellular Ca^{2+} levels in epithelial cells surrounding the MCs and SCCs were inhibited by muscarinic ACh antagonist atropine. Our results suggest that MCs and SCCs share common physiological roles in sensing chemical stimuli and may release ACh to influence surrounding non-sensory cells via paracrine mechanism. Because MCs lack afferent innervation, this cholinergic paracrine regulation could be especially important for chemoreception-mediated regulation of MOE activities. Acknowledgements: Supported by research grants NIH/NIDCD 009269, 012831 and ARRA administrative supplement to WL

#P118 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Long-term acclimation to capsaicin solutions affects taste bud volume and consumption in rats

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The effects of chronic exposure to capsaicin (the component responsible for the piquancy of chili peppers) in the gustatory system are not yet well understood; a critical consideration given capsaicin's popularity in culinary and medicinal applications. To examine these potential effects, rats received 40 days of treatment with a 30% sucrose solution containing either a 5 ppm capsaicin (in 2.5% ethanol) or sham (2.5% ethanol) condition. Animals began exposure as neonates (P5) or adults (P40) to evaluate potential differences across development. Taste bud volumes within fungiform papillae were measured at either two or 50 days post treatment, to assess immediate or lasting effects. Animals treated with capsaicin as neonates had significantly smaller taste buds at 50 days post treatment but in no other group (neonate or adult) were there significant differences. Capsaicin is a trigeminal irritant and does not directly affect the chorda tympani-innervated taste buds, thus the difference in taste bud volumes following capsaicin exposure suggests an integrated relationship between the chorda tympani and lingual nerves in gustatory maintenance. The capsaicin concentrations used here were significantly lower than those found in nature, as treatments were limited to what animals would consume willingly. As an additional experiment, we examined whether rats develop a tolerance to capsaicin over time. To do so we gave adult animals 5 ppm capsaicin/30% sucrose solutions and then incrementally increased the quantity of capsaicin by 2.5 ppm after each 5 day period. Initial results showed animals willingly consumed higher levels of capsaicin (10 ppm) with this type of acclimation. Taste bud volume analyses for these animals will be presented, and further experiments with additional acclimation are ongoing. Acknowledgements: University of Nebraska at Omaha: Graduate Research and Creative Activities Fund

#P119 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Trigeminal Mediation of Mammalian Aversion to Insect Chemical Defense Compounds

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Insects release defensive chemicals as one mechanism for deterring predation and defending their territory. A wide variety of insects use the same chemicals for this purpose. We hypothesize that defensive insect chemicals used by multiple insect orders are targeting the mammalian trigeminal system and eliciting chemesthesis. In the current study, we test a number of insect defense compounds to determine if they are irritating to a mammalian predator (rat). We first determined if these defense compounds activated the trigeminal nerve by recording from the ethmoid branch and monitoring respiration while perfusing stimuli through the rat's nasal cavity. Using these methods, we determined that all of the tested compounds except tetradecane activate the rat trigeminal nerve. Then, we examined behavioral aversion responses to these compounds by placing a rat in a square plexiglass arena with petri dishes in each corner. After a period of habituation, an insect chemical defense compound was added to one of the four petri dishes and the movement of the rat recorded. Ethovision XT (Noldus) was used to analyze whether rats spent less time in the irritant containing corner. Rats were behaviorally averse to most compounds at concentrations similar to those released by insects. By imaging primary cultures of rat trigeminal ganglia using a calcium responsive dye, we have confirmed the activation of the trigeminal system by insect chemical defense compounds. Additional experiments are underway to determine the specific receptor targets of these chemicals using a heterologous expression system. In the future, we will be doing similar work with chickens to determine the role of the trigeminal system in avian responses to insect defense compounds. Acknowledgements: WFU Center for Molecular Communication and Signaling

#P120 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Cholingeric Neurotransmission Links Solitary Chemosensory Cells To Nasal Inflammation

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Solitary chemosensory cells (SCCs) are specialized epithelial chemosensors that respond to "bitter" substances via the canonical taste transduction cascade (T2Rs, Gα-gustducin and TRPM5). When stimulated, SCCs release a hitherto unidentified neurotransmitter onto peptidergic nociceptive trigeminal fibers. Activation of these nociceptive fibers triggers neurogenic inflammation via NK1 (substance P) receptors on capillaries causing local plasma extravasation (Tizzano & Finger, AChemS 2012). How SCCs activate nerve fibers is unknown. In the present study, we show that choline acetyltransferase, the synthetic enzyme for acetylcholine (ACh), is present in SCCs. Previous studies have shown nicotinic ACh receptors (nAChR) on trigeminal fibers. Thus, all elements for cholinergic neurotransmission are present in the SCC-trigeminal system. To test if SCC-mediated inflammation requires activation of nAChRs, we measured SCC-evoked plasma extravasation in mice stimulated unilaterally with denatonium benzoate (20 μL, 10mM). Prior to chemical stimulation, mice were injected i.p. with either saline or the nAChR-antagonist Mecamylamine (Mec). Under urethane anesthesia, the right naris was stimulated with denatonium, and the mouse injected i.v. with Alexa555-conjugated albumin. Heads were bisected and fluorescence

intensity in the nasal epithelium was quantified. A one-way ANOVA demonstrated a significant difference between the three experimental groups [$F(2,12)=17.03$; $p<0.001$], with the saline control showing significantly more extravasation than either the 3mg/kg Mec [$p<0.01$] and 6 mg/kg Mec [$p<0.001$] groups (Tukey's HSD test). This result supports the hypothesis that SCCs are cholinergic, like tracheal brush cells (Krasteva , PNAS 2011), and release ACh to activate nAChRs on trigeminal fibers when stimulated. Acknowledgements: NIDCD R03 DC012413 (M.T.), R01 DC009820 (T.E.F.), and P30 DC04657 (to D. Restrepo)

#P121 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Both *painless* and *dTRPA1*, *Drosophila* TRPA Channels, Detect Chemical Irritants

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The ability to detect chemical irritants is important for the avoidance of potentially life threatening compounds. In mammals, one target of these irritants is the TRPA1 channel. The fruit fly, *Drosophila*, has four homologs of mammalian TRPA1, two of which are *painless* and *dTRPA1*. Previous research has provided contradictory evidence about the roles of *painless* and *dTRPA1* in fly chemical nociception. We used the proboscis extension reflex and developed a two-bottle preference test to analyze the behavioral phenotypes of *painless* and *dTRPA1* mutants. Both assays indicate that each channel is required for the behavioral aversion to AITC, though it is not clear whether they are acting independently or in combination. We evaluated the expression patterns of *painless* and *dTRPA1* to determine if there was colocalization. No overlap was seen centrally, and we are currently evaluating colocalization peripherally. To further define these cell populations, specific cell markers were identified. We observed subsets of *painless* and *dTRPA1* that were colocalized with the fly homologs of mammalian CGRP and Substance P, respectively. Cell excitability of *painless* and *dTRPA1* cells was assessed by using a Ca^{+2} reporter, GCaMP, to observe changes in Ca^{+2} levels in response to AITC. Both *painless* and *dTRPA1*-expressing cells displayed significant increases in fluorescence following application of AITC. To determine if activation occurred directly or indirectly, *painless* and *dTRPA1* were expressed in an ectopic *Drosophila* tissue. Again, both *painless* and *dTRPA1* demonstrated increases in cell excitability to AITC, suggesting that these channels are acting independently to detect irritants. Collectively, our results suggest a complex neural circuit that requires both the *painless* and *dTRPA1* channels for chemical nociception.

#P122 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

The Perception of Novel Cooling Ingredients in Flavored Beverages Varies with Ethnicity and Prior Experience

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Derivatives of l-menthol are cooling ingredients that are widely used in confectionery and oral care, and may have applications in beverages. To our knowledge, no studies have examined ethnic differences and prior experience with cooling ingredients in the sensory perception of cooling in model beverages. This study examined the oral sensations of cooling, heat/burning, tingling, sweetness, bitterness and overall flavor from lemon-lime flavored beverages with two novel cooling ingredient blends; Coolact® 38D/(l)-menthyl lactate blend or Coolact® 5 /Coolact®10 blend in healthy adults who were East Asian (n=54), Caucasian (n=43) or other (n=19). Subjects rated intensity and liking of each blend at four concentrations (0, 75, 150, and 300 ppm) using 15-cm line scales at four time points (0, 2.5, 5 and 10 min) after tasting. The intensity of all attributes was maximal immediately after tasting ($P<0.0001$) and decreased with time ($p<0.0001$). Both blends primarily delivered the sensations of cooling and tingling with minimal perception of heat/burning and bitterness. At time 0, East Asians perceived more heat/burning than Caucasians from Coolact®5 / Coolact®10 blend ($p<0.01$). Also, subjects who were familiar with flavored beverages containing cooling ingredients (n=60) perceived more cooling, heat/burning and tingling from the Coolact®5 / Coolact®10 blend ($p<0.0001$) and more cooling ($p<0.001$) and heat/burning ($p<0.01$) from the Coolact® 38D / (l)-menthyl lactate blend compared to subjects who were not familiar with these products (n=56). These data suggest that the intensity of cooling ingredients in beverages is influenced by ethnicity and prior experience with these beverages.These factors should be considered in future psychophysical studies of cooling ingredients and product applications Acknowledgements: Supported by Takasago International Corporation (U.S.A.).

#P123 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Peptidergic Trigeminal Nerve Fibers are Required for Solitary Chemosensory Cell-mediated inflammation following chemical insult of the nasal mucosa

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The nasal epithelium houses a population of solitary chemosensory cells (SCCs) that express T2R taste receptors along with their downstream signaling components and which are heavily innervated by peptidergic (substance P) trigeminal

nerve fibers. Nasal SCCs respond to bitter compounds including bacterially-produced molecules, to evoke protective respiratory reflexes and early inflammatory responses (Gulbransen 2008, Tizzano 2010 and AChemS 2012). Here we test whether SCC-mediated pro-inflammatory responses require activation of the trigeminal nerve and subsequent peptidergic neurotransmission, or whether SCC activation triggers local inflammation via an intramucosal paracrine signaling mechanism. When denatonium (10mM) is instilled into the nasal passageways, it evokes SCC-dependent plasma leakage and local mast cell (MC) degranulation (Tizzano AChemS 2012). Chemical ablation of peptidergic nerve fibers with resiniferatoxin (RTX, an ultrapotent analog of capsaicin) eliminates both denatonium-mediated plasma leakage and MC degranulation. These results show that the peptidergic nerve fibers are necessary for these SCC-mediated pro-inflammatory events. Moreover, injection of L732138 (5mg/kg), an inhibitor of the neurokinin 1 (substance P) receptor present on blood vessels, prevents denatonium-induced plasma leakage. This indicates that substance P is the mediator for plasma leakage. Our results demonstrate that activation of the SCCs leads to a rapid, local pro-inflammatory response via neurogenic mechanisms. This fast pro-inflammatory response, driven by the SCCs in conjunction with the trigeminal nerve, represents a 1st line of defense against respiratory epithelial assault by noxious chemicals and bacterial pathogens. Acknowledgements: NIDCD R03 DC012413 (M.T.), R01 DC009820 (T.E.F.), and P30 DC04657 (to D. Restrepo)

#P124 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

The Influence of Bubbles on the Perception of Carbonation Bite

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Although many people assume that the bite of carbonation is due to tactile stimulation of the oral cavity by bubbles, it has become increasingly clear that carbonation bite comes mainly from formation of carbonic acid in the oral mucosa. In Experiment 1, we asked whether bubbles were in fact required to perceive carbonation bite. Subjects rated oral pungency from several concentrations of carbonated water both at normal atmospheric pressure (at which bubbles could form) and at 2.0 atmospheres pressure (at which bubbles did not form). Ratings of carbonation bite under the two pressure conditions were essentially identical, indicating that bubbles are not required for pungency. In Experiment 2, we created controlled streams of air bubbles around the tongue in mildly pungent CO_2 solutions to determine how tactile stimulation from bubbles affects carbonation bite. Since innocuous sensations like light touch and cooling often suppress pain, we predicted that bubbles might reduce rated bite. Contrary to prediction, air bubbles flowing around the tongue significantly enhanced rated bite, without inducing perceived bite in blank (un-carbonated) solutions. Accordingly, though bubbles are clearly not required for carbonation bite, they may well modulate perceived bite. More generally, the results show that innocuous tactile stimulation can enhance chemogenic pain. Possible physiological mechanisms are discussed. Acknowledgements: Supported in part by Anheuser-Busch InBev

#P125 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Acid detection by TRPV1 channels in both 'taste blind' (P2X-KO) and C57 mice

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In the oropharynx the low pH of acidic solutions is detected via taste as sour, and by general mucosal fibers as pungency or chemesthesis. This results in the behavioral avoidance of acidic stimuli but the relative contribution of these two systems is unknown. Genetic deletion of the purinergic receptors P2X2 and P2X3 (P2X-KO) results in interruption of taste bud-to-nerve transmission and consequent loss of taste responses in the gustatory nerves. Although P2X-KO mice do not respond behaviorally to most tastants, they continue to avoid acids at similar concentrations as wildtypes. General mucosal afferents express TRPV1 channels, which are activated by low pH and may underlie this avoidance of acids. To test this, P2X-KO (n=8) and C57 (n=12) mice were assessed using a two-bottle preference test in which one bottle contained 20 mM citric acid (CA) and the other water. The test was given in the presence and absence of the TRPV1 antagonist Iodoresiniferatoxin (I-RTX). Both strains showed a significant decrease in avoidance with I-RTX versus vehicle ($p<0.05$) indicating a role for TRPV1 in acid avoidance. Additionally, C57 mice that had been injected repeatedly with Resiniferatoxin (RTX) to eliminate TRPV1 nerve terminals were tested using a two-bottle preference test with 20 mM CA and water. The RTX injected mice had a higher acid intake, 19%, than controls, 11%. This difference was similar to the change in acid intake of C57 mice given I-RTX, 21%, versus vehicle, 12%. These results indicate that the TRPV1 channel is important in non-taste acid avoidance. However, P2X-KO mice still avoided CA even with the TRPV1 channel blocked suggesting that TRPV1 does not account for all non-taste acid detection and that other mechanisms are likely involved, e.g. TRPA1 (Wang et al. 2011). Acknowledgements: Supported by NIH Grant R56DC000147 (TEF) and P30 DC04657 (Rocky Mountain Taste & Smell Center).

#P126 POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY

N-geranylcyclopropylcaboximide (NGCC) selectively activate hTRPV1 and hTRPA1 in cultured cells

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In mammals, two salt taste pathways have been characterized: one is selectively responsive to Na^+, which is inhibited by amiloride and the other is Na^+ non-specific and amiloride-insensitive. As the amiloride-sensitive Na^+ specific salt taste receptor, the epithelial sodium channel (ENaC) has been validated. The transient receptor potential vanilloid-1 variant salt taste receptor (TRPV1t) has been proposed as a constitutively active non-selective cation channel that has many similarities with the pain receptor TRPV1. In previous report we have shown that NGCC synthesized by IFF, modulates salt taste on human and amiloride-insensitive NaCl chorda tympani taste nerve responses by interacting with TRPV1t. In this presentation, we performed calcium imaging and cell based assay using in hTRPV1-expressing cells to test the interaction with NGCC and TRPV1NGCC enhanced Ca^{2+} influx in hTRPV1-exrpessing cells in a time- and dose-dependent manner with an EC_{50} value of 98.7 μM. The NGCC-induced Ca^{2+} influx was markedly attenuated by ruthenium red (30 μM), a general blocker of TRP channels, and capsazepine (5 μM), a specific antagonist of TRPV1, implying NGCC directly activate TRPV1. On the other hand, TRPA1 is often co-expressed with TRPV1 in sensory neurons therefore we investigated the effects of NGCC on hTRPA1-expressing cells. NGCC enhanced Ca^{2+} influx in hTRPA1-exrpessing cells in the same manner as in hTRPV1 with an EC50 value of 57.2 μM. The NGCC-induced Ca^{2+} influx was blocked by ruthenium red (30 μM), and HC-030031 (100 μM), a specific antagonist of TRPA1. These data provides evidence that NGCC selectively activate TRPV1 and TRPA1 in cultured cells. These data further support our previous suggestion that NGCC interact with the TRPV1 variant cation channel in the anterior taste receptive field. Acknowledgements: Supported by a Korea Food Research Institute (KFRI) grant E0121201 and DC-011569

#P127 POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY

Olfactory Overshadowing: The Effect of Verbal and Tactile Stimuli on Olfactory Memory

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While the strong association between smell and memory has received considerable attention, little is understood about the effect non-olfactory stimuli have on the encoding of olfactory memory. In the "verbal overshadowing" part of this study, subjects were divided into 5 groups which differed in the type of verbal response attached to 10 target odors presented during a training phase. In the 4 experimental groups, subjects verbalized names or descriptors whereas subjects in the control group provided no verbal name or description. After participating in an unrelated task, subjects were presented with a battery of odorants one at a time (10 targets and 10 distracters) and asked if they remembered smelling each odorant. Subjects who verbalized a name or description recognized fewer odorants as compared to subjects who provided no verbal response. In addition, the subjects who provided no verbal response identified fewer distracter odorants as belonging to the target group. In the "temperature overshadowing" part of this study, subjects had cold or room temperature water applied to their hands while they concurrently smelled the target odors. Subjects who had water applied to their hands during the training phase recognized fewer of the target odorants as compared to subjects in a control group from the verbal overshadowing part of the study who had no water applied to their hands; additionally subjects recalled fewer of the odors that were paired with the cold stimulus than those that were paired with room temperature water. The data from both parts of this study is consistent with the hypothesis that olfactory memory is impaired when target odorants are coupled with verbal or tactile stimuli. Acknowledgements:
The St. Lawrence University Fellows Program and the Biology Department provided some of the funding for this work.

#P128 POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY

A new paradigm for testing olfactory memory performance in healthy humans

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Long-term memory processes can be divided into two categories: declarative and procedural memory. While declarative memory concerns actual knowledge of facts, procedural memory applies to more unconscious memory of abilities and skills. Declarative memory processes are based upon the two components recollection and recognition. Odors are considered highly salient but abstract evocative cues during the recollection of past personal experiences and events. The aim of our current

study was to develop a paradigm for testing declarative memory processes with regard to odors. Therefore, we implemented three memory tasks in E-prime 2.0 presentation software. With help of an odor-place associative memory task we investigated memory of odor-place combinations. During an odor item recognition task the subjects were asked if they had experienced several odors during the previous task. As a control task for the first task a picture-place associative memory task was utilized. Each of those tasks contained two phases – an encoding phase (1 block) and a retrieval phase (4 blocks) – and were applied to 17 healthy subjects. The results suggest that the subjects were able to learn during the encoding as well as during the retrieval phase. We found higher odor-place associative, odor recognition, and picture-place associative memory performance scores at the end compared to the beginning of the retrieval phase. We thus claim that our paradigm renders useful during the investigation of olfactory memory processes and the influence of external factors on those processes in humans. We here present a fully automated paradigm, which can be utilized during future functional imaging studies with the goal to shed light onto the neural network of human olfactory memory processes. Acknowledgements: This research was funded by a startup grant from the Medical Faculty of RWTH Aachen University.

#P129 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Fragrance Materials Extend the Range of a Model for Odor Potency

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Olfactory research offers few trustworthy odor thresholds. Bad for the field, the situation sets nonexperts in need of the information adrift. A rule of thumb says to choose the lowest threshold of a set because studies with the best stimulus control and some measure of concentration normally yield the lowest values. Nagata et al. over years produced the largest set of thresholds gathered with coherent methodology and analytical verification. They lie below most others. Abraham et al. used a well-established linear solvation energy relationship (LSER) to describe the set. To strengthen the position, they incorporated sets from the CPL and Hellman. Data obtained via olfactometer in recent years from the CPL needed no normalization with the Nagata set, whereas those from Hellman and earlier squeeze-bottle data from the CPL did. The LSER accommodated these via indicator variables (factors) to bring the data into line and described potency for 353 odorants. Although the equation left about 25% of variance unaccounted for, it offers the strongest statement yet for prediction. Until now, no sets included fragrance materials, such as patchouli oil or vanillin, known for potency. Without them, one could argue that the equation might describe local rather than universal rules. We accordingly ran groups of at least 10 Ss on over a dozen such materials. We used the CPL protocols that have given stable results and required no normalization. The outcome fell in line with the data for the hundreds of materials, with neither more nor less variance. It adds evidence that the LSER has universal relevance to predict potency. Since the solvation-relevant parameters used for prediction exist for thousands of materials, the LSER may afford more accessibility and accuracy than values in compilations. Acknowledgements: Supported by International Flavors and Fragrances.

#P130 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Categorical Dimensions of Human Odor Descriptor Space Revealed by Non-Negative Matrix Factorization

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Recent studies using Principal Components Analysis (PCA) support low-dimensional models of odor space, in which one or two dimensions – with hedonic valence featuring prominently – explain most odor variability. Here we use non-negative matrix factorization (NMF) – a nonlinear optimization method - to discover an alternative, reduced-dimensional representation of the Dravnieks odor database(144 odors x 146 descriptors). We first divided the dataset into training and testing halves, and found that RMSD testing error attained a minimum for subspace choice of 25, motivating this as an upper bound for odor perceptual space dimensionality. More parsimonious representations were found by comparing reconstruction errors (fraction of unexplained variance) of NMF with reconstruction errors of PCA on scrambled data (PCAsd). For subspace sizes > 10, NMF error was indistinguishable from PCAsd error, indicating no gain in retaining more than 10 perceptual dimensions. As is typical of NMF basis sets, the 10 odor dimensions we obtain are sparse (only a small subset of the 146 descriptors apply), and categorical (represent a positive valued quality). Moreover, these 10 dimensions were near-orthogonal, with a mean angle of 73 degrees between all pairs of basis vectors. Investigating the distribution of odors in this 10-dimensional space, we find marked clustering, with each odor clearly defined by its membership in a single dimension, to the exclusion of others. Members of each cluster have notable structural homology, which we quantified as correlations among physiochemical descriptors of odors in each cluster. In sum, we describe a representation of odor perceptual space consisting of 10 discretely occupied dimensions that apply categorically. We propose that this may help elucidate the natural axes of olfaction. Acknowledgements: NIH GM086238 (CSC)

#P131 POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY

Genetic Contribution to Binaral Rivalry

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When two odorants of different structure and smell are simultaneously presented to the two nostrils, we experience alternations in olfactory percepts, a recently discovered phenomenon termed binaral rivalry. In an effort to further characterize this phenomenon and its nature, we adopted the twin method and tested monozygotic (MZ) twins (n = 73 pairs) that are genetically identical and dizygotic (DZ) twins (n = 70 pairs) that share about half of their genes. The majority of participants experienced binaral rivalry over a course of 20 samplings of eugenol and amyl acetate, one to each nostril. Large variances are observed in the number and the magnitude of their perceptual switches. Critically, such individual differences are partially genetic. The correlations between MZ twins for the two aforementioned indexes are both higher than those between DZ twins. The best-fitting genetic models showed that over 30% of the variances in binaral rivalry rate and binaral rivalry magnitude, respectively, were accounted for by additive genetic factors. Our study represents the first large sample study of binaral rivalry. The findings demonstrate a reliable genetic component of this phenomenon and suggest an innate rhythm of olfactory perception.

#P132 POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY

Olfactory Plasticity in Young Adults

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There is considerable evidence that olfaction is, in many ways, a "learned" sense, showing experience-induced plasticity in both central circuits and peripheral receptors even in adulthood. Although this has been demonstrated in humans, the focus has been on single chemicals to which some individuals are initially insensitive. We sought to explore (1) the possibility of enhancing young adult sensitivity to complex odors, (2) the role of cognitive engagement (active identification of exposed odors vs. simple exposure), and (3) the extent of transfer of learning to unexposed odors. For this, we obtained both odor thresholds and olfactory event-related potentials (OERPs) from 40 young adults in an attempt to assess the neuronal mechanisms of potential behavioral changes. Thresholds for four exposed and two unexposed complex odorants were obtained at baseline, 6 and 12 weeks; OERPs in response to two of the exposed and both unexposed odorants were obtained at baseline and 12 weeks. Our behavioral results suggest that intermittent odor exposure in these circumstances does enhance threshold sensitivity and that cognitive engagement may further enhance generalization to unexposed odorants. Our electrophysiological results show learning-dependent amplitude changes, particularly of the late positive component. Taken together, these data provide further support for the notion that repeated exposure augments olfactory sensitivity and that cognitive mechanisms exert a significant modulatory effect. Acknowledgements: Supported by the U.S. Army Research Office, grant #W911NF-11-1-0087.

#P133 POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY

Proton-Transfer-Reaction Mass Spectrometry

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Since their introduction in the mid-1990s, Sniffin' Sticks have been used effectively by many otolaryngologists to assess olfactory dysfunction in countless patients. Despite their widespread use, however, there is currently a lack of data on the actual odorant concentrations released from the tips of these pens and whether these emitted concentrations scale linearly in accordance with the odorant concentrations of the pen set. The purpose of this study was to ascertain whether the Sniffin' Sticks' presumed odorant release was concordant with the concentration of the odorant solutions placed in the pens. The commercially-available odour threshold test containing n-butanol was chosen here for evaluation. The threshold set contains concentrations (v/v) ranging from 4 % (pen no. 1) to 1.2 ppm_v (pen no. 16), with stepwise 1:2 dilutions. We also tested an additional custom-made pen containing 8 % n-butanol (pen no. 0). The odorant concentration emanating from the tip of each pen was measured directly via proton-transfer-reaction mass spectrometry (PTR-MS), which is an on-line analytical tool for detection and quantitation of volatile organic compounds (VOCs) – including odorants – at trace concentrations. The pens were also subjected to repeated use to ascertain the degree of reproducibility of emitted odorant concentrations under stress. These measurements showed that the concentration linearity of n-butanol emitted over the range of pens was excellent and highly reproducible. The stress tests demonstrated that the emitted concentrations of n-butanol were lower after repeated use of the pens compared to those of the unused pens, albeit with a mostly good linearity over the entire range of pens. Acknowledgements: Part of this study is affiliated with the Neurotrition Project, which is supported by the FAU Emerging Fields Initiative. This

work was also partly supported by The National Social Life, Health and Aging Project Wave 2 (R37 AG030481). DWK is supported by The Center on Aging Specialized Training Program in the Demography and Economics of Aging, which is funded by the National Institute on Aging (NIA) (T32000243)

#P134 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Effects of Cinnamon Scent Administration on Physiology, Range of Motion, Mood, Anxiety and Perceived Workload During a Multi-session Physical Therapy Program

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Scents have been shown to elicit both emotional and physiological responses. The current study aimed to evaluate the possible effects of cinnamon scent when applied to a physical therapy regimen. Forty-two undergraduate students, 16 males and 26 female, completed a four trial physical therapy regimen in one of two rooms: a control room or a room infused with a cinnamon scent. The experimenters measured participants' range of motion, mood (POMS), and anxiety (STAI) prior to and following each trial of exercises. At the end of each visit, perceived workload was assessed (NASA-TLX). The data were analyzed using a 4 (visits) X 2 (groups) mixed design ANOVA. Significant results were found for ratings of effort on the NASA-TLX, $F(3, 120)=2.8$, $p = .042$. Participants in the cinnamon scent condition rated their perceived effort exertion as being lower than participants in the control condition. Decreased perceived effort may cause patients undergoing a physical therapy program to feel more comfortable while completing their exercises, thus increasing the likelihood of adherence to the program.

#P135 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Towards A Novel Method for Human Olfactory Research

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The majority of human olfactory research to date has been conducted without regard to perfume or dietary contributions to body odor. Given that humans have used perfume for thousands of years, and that culturally mediated food preferences may affect body odor, I propose that an ecologically relevant model of olfactory communication should account for body odor as people present themselves in real social situations. Further, current collection methods for odor samples focus mainly on axillary secretions, though it is known that other body areas contribute to odor. This pilot study aims to validate a novel olfactory research method by employing present others rather than disembodied odors. In a repeated measures design, blindfolded, ear-plugged raters evaluated a series of participants as each sat beside them. No restrictions in diet or fragrance were used, to mimic real-life interactions. First and second ratings for each participant were examined for intertrial reliability, revealing significant consistency ($p<.001$), even though raters were unaware of our repeated measures design. Self-report measures of odor sensitivity, perfume usage, and perceived pleasantness of friends' body odors were significantly associated with pleasantness ratings ($p<.05$). These preliminary results indicate reliable olfactory perception of body odor in this novel design. Upcoming iterations will provide a larger sample size, and plans for future experiments include examining more typically purified body odor, as well as comparing purified to daily body odor, which will allow us to gain insight into the potential effects of fragrance and dietary choices on olfactory communication. Studies comparing lab samples to present others will evaluate the generalizability of tightly controlled lab techniques to real life situations. Acknowledgements: Institute for the Social Sciences, Cornell University

#P136 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Effects of Prediction and Control on the Perception of Aversive Olfactory Stimuli

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Prediction and control are distinct cognitive functions that have been shown to play significant roles in emotion regulation. Animal studies have demonstrated that the ability to predict or exert control over the temporal onset of aversive stimulus presentation substantially decreases stimulus-evoked physiological arousal. Whether these reductions in arousal are due to changes in the perception of the stimulus itself, however, is unknown. Here we examined the effects of prediction and control on responses to aversive olfactory stimuli in human subjects. The decision to use odorants as aversive stimuli was based on the intimate anatomical and functional connections between olfactory and limbic systems—olfactory sensory neurons are only two synapses removed from brain areas involved in emotion. Subjects were presented with aversive olfactory stimuli whose onset time was either predictable, controllable, or neither. Responses to olfactory stimuli included self-report ratings of anticipatory anxiety and odorant aversiveness as well as stimulus-evoked physiological arousal (i.e., skin conductance response). Critically, subjects received the same duration and frequency of aversive stimulus delivery in each condition, and olfactory stimuli were matched for valence and familiarity across all conditions. As hypothesized, results indicated that subjects' responses to aversive olfactory stimuli differed depending on whether stimuli were presented in a predictable or controllable manner, despite no change in the frequency or duration of stimulus presentation. Follow-up fMRI research examining potential roles of the medial prefrontal

cortex during control versus prediction is currently underway and will also be discussed. Acknowledgements: The research in this presentation is supported by the National Institutes of Health [NIDCD 1 R01 DC 010014, NIMH 5 F32 MH 091967].

#P137 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Pleasant and unpleasant odors are easier to detect and harder to ignore

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Odor objects are often experienced within the context of several competing odors. To deal with the excess of information the olfactory system utilizes mechanisms that bias the competition between odors towards preferential representation of the most relevant odor. This biasing may involve anticipatory attentional mechanisms that use feature-related information regarding behaviorally relevant odors to amplify relevant odors and filter our irrelevant odors. Since an important feature of olfactory stimuli is their valence, the present study utilized an olfactory attentional search task to examine whether 1) expectation of pleasant or unpleasant odors enhances perceptual sensitivity compared to neutral odors and 2) presence of an irrelevant pleasant or unpleasant odor make it harder to detect a relevant odor. Subjects performed an olfactory task in which they decided whether a particular target smell is present in each trial. Trials started with a cue that indicated the forthcoming target odor (pleasant odor A, unpleasant odor B, or neutral odor C) followed by the target stimulus. The stimulus consisted of either odor A alone, odor B alone, odor C alone, or binary mixture of these odors (AB, AC, and BC). In our results,d-prime, a measure of perceptual sensitivity showed the following trend: pleasant odor following pleasant cues > unpleasant odors following unpleasant cues > neutral odors following neutral cues ($F(1,13)=7.240$, $p<0.05$). Furthermore, accuracy for detection of target odor was impaired when presented in a mixture consisting of an unpleasant or pleasant odor ($F(1,13)=33.539$, $p<0.001$). Present findings shed light on how emotional valence and selective attentional mechanisms interact to impact the perception of olfactory objects.

#P138 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Vanilla and Olfaction

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The purpose of this research is to establish norms for the odorant vanilla by using the University of Pennsylvania Smell Identification Test (UPSIT), a norm referenced test of odor detection, as a template. Additionally, the odorants of banana and menthol, included on the UPSIT, were sampled to use as a base for comparing relative equivalency of the norm sample. Banana was chosen from amongst other UPSIT odorants due to the somewhat similar sweet smell as compared to vanilla and menthol was chosen based on the involvement of the fifth cranial nerve in processing this odorant. Vanilla was chosen due to evidence that it may be preferred in infancy. Marchlewska-Koj, Lepri, and Muller-Schwarze (2001) found that premature infants showed a higher respiratory response to vanilla during stimulation and no response to butyric acid. Savic-Burgland (2004) using positron-emission tomographic scanning (PET scanning) showed that vanilla was processed differently. For example, vanilla was found to influence only half of the olfactory nerve. Results of the three odorants sampled by 380 of subjects showed that banana and menthol had a correct identification rate of 59.7% and 88.9%, respectively, and vanilla had a 74.3% correct identification rate. The importance of including vanilla as an odorant in smell identification tests used to screen olfaction dysfunction is supported by this research. Acknowledgements: Wheeler Center for Odor Research

#P139 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Odorant Measurement at the Olfactory Cleft using Proton-Transfer-Reaction Mass Spectrometry

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Olfactory detection and threshold sensitivity is traditionally based on the concentration of the stimulus-odorant solution, and does not typically consider the chemical concentration of the stimulus-odorant at the level of the olfactory receptors. Here we report a technique for directly measuring odorant concentration in the olfactory cleft, utilizing Proton-Transfer-Reaction Mass Spectrometry (PTR-MS). PTR-MS samples were collected using an approximately 15 cm long PVC catheter (outer diameter:

3.3 mm) placed at the olfactory cleft under endoscopic guidance. Participants did not require topical anaesthetics or decongestants and sniffed naturally (n=35; 21 female, 32±7 years of age). An additional cannula fitted at the nostrils was connected to a pressure transducer to record inspiratory nasal pressure and breathing cycles throughout odorant presentation. Following a protocol similar to that which is used during clinical assessments, n-butanol was presented in a triad of Sniffin' Sticks pens, 1 odorant target pen and 2 'odorless' blanks. Participants were asked to identify the odorant-containing target pen in each of six triads with increasing n-butanol concentrations (0.125, 0.25, 0.5, 2, 4, and 8 %). The entire protocol only required approximately 15 minutes to perform. All participants were fully compliant and reported only minimal discomfort. The catheter and cannula did not disrupt normal breathing patterns. This protocol allowed us to quickly and effectively measure odorant concentrations at the olfactory cleft in real time. Comparing the known concentration of the stimulus odorant and the concentration found at the olfactory cleft will elucidate how to best adjust and develop measures designed to determine an individual's threshold sensitivity. Acknowledgements: This work was supported in part by The National Social Life, Health and Aging Project Wave 2 (R37 AG030481), and is affiliated with the Neurotrition Project, supported by the FAU Emerging Fields Initiative. DWK is supported by The Center on Aging Specialized Training Program in the Demography and Economics of Aging (National Institute on Aging (T32000243). TH received funding from the DFG (HU 441/10-1).

#P140 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Quantitative classification of the perceived intensity curve of a continuously presented odor

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Researchers of olfaction have devoted significant effort to understanding the phenomenon of adaptation. Previous studies of olfactory adaptation have reported, in general, that perceived intensity of a continuously presented odor decreases exponentially over time. More recently, however, other studies have shown that perceived intensity of continuous odor does not always decrease exponentially. Some studies focused on the various time-course of perceived intensity of a continuously presented odor, whereas few studies have tried to classify time-course patterns quantitatively. In this study, we performed real-time evaluation of perceived intensity of a continuously presented odor for 480 seconds using nine odorants, and quantitatively classified the perceived intensity curves using the time points for 20-80% of time integral of perceived intensity. This analysis revealed that intensity curves could be classified into two clusters: one group ("typical") exhibited the commonly observed exponential decrease in perceived intensity; the other group ("non-typical") included a range of time courses rather than strict exponential decrease. The average intensity of "typical" group decreased below threshold three minutes after beginning of odor exposure, and that of "non-typical" group, on the other hand, did not decrease under threshold during total measuring time.

#P141 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Effects of Peppermint Scent Administration on Augmenting Cognitive and Creative Performance

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Level of creativity has been assessed in a number of ways, including interactions between body and environment on creative thinking. Environmental richness has been shown to interact with creativity, with greater levels of environmental richness leading to more creative responses. The present study attempted to determine if peppermint scent administration could promote creativity, since past research with peppermint scent reports improved performance on clerical tests, thus hinting at the possibility for cognitive enhancement. Participants completed the Torrance® Tests of Creative Thinking, a standardized test measuring creative thinking abilities, in both a non-scented condition (control) and a peppermint scented condition. Different versions of the test, as well as the conditions, were counterbalanced. The data were subjected to paired samples t-tests, with condition (peppermint, control) serving as the independent measure and raw scores of fluency, originality, elaboration, abstractness-of-titles, and resistance-to-premature-closure serving as dependant measures. There was a significant difference between the conditions for fluency [t(33)=-2.41, p=.02], originality [t(33)=-2.13, p=.04], and elaboration [t(33)=-7.38, p=.00], with all measures having higher scores for the peppermint scent condition. Implications suggest working conditions for those individuals with occupations that require creative thinking and problem solving may benefit from peppermint scented working conditions.

#P142 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Contextual effects on hedonic evaluation of odors

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When we sequentially evaluate a character of sensory modality stimuli, evaluation of the stimuli might be influenced by what precedes them; contextual effects. Hedonic contrast, is one of these phenomenon, when a stimulus is preceded by a more pleasant stimulus, its pleasantness is rated lower (negative contrast), whereas when a stimulus is preceded by a less pleasant stimulus, its pleasantness is rated higher (positive contrast).

In this study, we investigated the contrast effect during evaluation of odor intensity and pleasantness. Two sets of positive odors and a set of negative odors were used. Group 1 sequentially rated the positive set A, the negative set, and the positive set B. Group 2 rated the negative set and then the positive set B. Group 3 rated only the positive set B. The mean rating of the negative and the positive set B were each compared among groups. As a result, in the intensity rating, both positive and negative contrast occurred clearly. In the pleasantness rating, only negative contrast was seen. This suggested that, in olfaction, the influence of the positive context stimuli on the following negative stimuli might be more robust. To investigate the cause of the non-occurrence of positive contrast, we analyzed a change of hedonic evaluation by rating order within a positive or negative set. While there was no influence of the rating order in a negative set, the pleasantness rating of a positive set tended to gradually decrease. This result is discussed in terms of the unstable characteristics for hedonic evaluation of positive odors and the stability of the hedonic rating of negative odors. Therefore, positive hedonic contrast may not occur due to the hedonic value of negative odors being carried over to the following rating of the better stimuli.

#P143 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Increased cortisol secretion after awakening following lavender inhalation during sleep

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Aromatherapy improves sleep through autonomous nervous system (ANS) modulation. However, few studies have focused on the effect of olfactory exposure during sleep on hormonal secretion. The objective of this study was to investigate the effect of inhaling odorants on cortisol secretion during sleep and after awakening. Salivary cortisol was assessed because this glucocorticoid represents activation of the hypothalamus-pituitary-adrenal (HPA) system, which is a dominant stress reaction pathway in the body. We used essential oils of jasmine and lavender, which induce activation of the sympathetic and parasympathetic nervous systems (PSNS), respectively. These oils were administered to subjects through an olfactometer; volatilized odorants were intermittently delivered through a cannula (first 1 min of each 5 min interval) during a 6-h sleep period. Subjects experienced each odorant condition [jasmine, lavender, or scentless air (control) each night] and were exposed to all three conditions in a counter-balanced order. Saliva samples were collected every 30 min while the subjects were asleep using our own-developed saliva collection equipment and every 15 min for 1 h after awakening. Surprisingly, salivary cortisol after awakening was significantly higher under the lavender condition than in the jasmine ($p < .01$) or control ($p < .05$) conditions, whereas no difference in cortisol secretion was observed while the subjects were asleep. Although lavender has a sedative effect on humans thorough the activation of PSNS, inhaling this popular aroma during sleep may have a significant impact on cortisol secretion by enhancing HPA activity after awakening.

#P144 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Common aversive learning mechanisms to olfactory and visual stimuli

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Learning to avoid dangers is an evolutionary problem that all organisms must solve. Aversive learning is a mechanism mediating the acquisition of conditioned responses (CR), but it also alters the perception of the predictive cue, allowing a differentiation of "threatening" and "safe" stimuli. It has been debated whether CRs to odors are stronger than to other sensory stimuli. We here investigated whether increased conditioning to olfactory stimuli could be related to an increased orienting response to odors due to their relative sparseness compared to visual stimuli in our everyday environment. Twenty participants were tested employing repeated conditioning (5 reinforcement sessions) of the same olfactory and visual stimuli over a period of two weeks and compared to 20 matched individuals that only were exposed to one acquisition session. Although odor stimuli demonstrated a larger initial CR than visual stimuli consistent with an initially increased orienting response, this difference disappeared after repeated reinforcement sessions, suggesting the presence of sensory independent aversive learning mechanisms. In conclusion, the strength of aversive conditioning is similar to olfactory and visual stimuli suggesting a common neural circuitry underlying aversive conditioning. These findings provide a framework for understanding perceptual processing in anxiety disorders. Acknowledgements: This material is based upon work supported by the U. S. Army Research Office under grant number W911NF-11-1-0087

#P145 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Perception of large and small odorant molecules – A study investigating the olfactory perception as a function of age and odorant molecular size

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For various sensory systems selective functional limitations with increasing age were detected. In vision and hearing it shows in hyperopia or an increased hearing threshold for high frequencies. But what about the olfactory system? While some studies suggest a general olfactory impairment, others allow assumptions of partial processes. In this study the influence of odorant molecular size was examined for the olfactory perception in different ages. Olfactory threshold tests were conducted at two age groups (group 1: 18 to 30 years, group 2: 50 to 70 years). We used single odorants, bimolecular odorants and perfumes, each consisting of large or small molecules. The results of these studies showed no differences for large and small odorant molecules in the young group of subjects. Whereas they were perceived differently by the 50 to 70 year-old. The latter had significantly higher thresholds for large olfactory molecules. This phenomenon however, was detected only for mono- and bimolecular odorants. Perfumes were perceived similar in both groups. In Conclusion we can hypothesize differing processes for odor perception of small and big odorant molecules in different age-groups at the receptor level. Moreover perfumes seem to generate more complex olfactory information. The existence of partial processes on olfactory impairment with increasing age is expected for the olfactory system, too. Acknowledgements: This project was supported by a grant from DFG Schwerpunktprogramm (SPP) 1392 - Integrative Analysis of Olfaction to Thomas Hummel. In addition we thank Fragrance Resources GmbH, Hamburg for cooperation.

#P146 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Odor Identification and Cognition in a Nationally Representative Sample of Older Adults

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Errors in odor identification are associated with subsequent cognitive impairment in populations clinically at risk for Alzheimer and Parkinson diseases. However, such associations have not been investigated in the general U.S. population. We administered a 5-item test of odor identification to a U.S. national probability sample of 3,005 community-dwelling adults aged 57–85 in 2005–6 (Wave 1); respondents and their spouses were then retested in 2010–1 (Wave 2). Odors were presented using Sniffin' Sticks, and respondents were asked to identify each from among four word-picture options. Respondents in Wave 2 also completed the Chicago Cognitive Function Measure (C-CFM), a survey instrument assessing eight distinct cognitive domains, derived from the Montreal Cognitive Assessment (MoCA). The C-CFM is 30% faster, with scores ranging from 0–20 (mean = 13.5, SD = 4.1) that correlate highly with the MoCA (r = 0.97). In a multiple regression model of C-CFM on odor identification score in Wave 2 (n = 2,076), each additional odor identification error was associated with a reduction in C-CFM score of 0.61 (95% CI = (0.44, 0.77); p <0.001), even after controlling for age, gender, race/ethnicity, education and self-rated physical and mental health. The change in odor identification score over 5 years was also predictive of C-CFM scores in Wave 2, with each additional error (relative to Wave 1) corresponding to a reduction in C-CFM score of 0.29 (95% CI = (0.11, 0.47); p = 0.002). NSHAP is the first study to demonstrate an association between olfactory and cognitive function among the U.S. population of older adults. These results suggest that this relationship is not limited to those at high risk of neurodegenerative disease, but may also represent a more fundamental characteristic of the aging process. Acknowledgements: The National Social Life, Health and Aging Project Wave 2 (R37 AG030481). DWK is supported by The Center on Aging Specialized Training Program in the Demography and Economics of Aging, which is funded by the National Institute on Aging (NIA) (T32000243). JMP was supported by the Institute of Translational Medicine at The University of Chicago (KL2RR025000) and the National Institute on Aging (AG036762).

#P147 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Longitudinal Study of Olfactory Decline in a Nationally Representative Sample of Community Dwelling Older Adults

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In a cross-sectional study we previously demonstrated striking race and gender differences in olfactory function among older US adults (AChems 2012). Here we report a 5 year follow-up of the same subjects to determine 1) the rate of olfactory decline and 2) if this decline differed by race or gender. The National Social Life, Health and Aging Project (NSHAP) interviewed a nationally-representative sample of community-dwelling older US adults (57-85 years) in 2005-6 (Wave 1) and in 2010-11

(Wave 2), assessing demographics, social life, and health, including olfaction (N = 1436). Odor identification was measured with 5 Sniffin' Sticks (0-5 correct). Multivariate linear regression quantified the association between olfactory decline over 5 years and demographic, health and psychosocial factors. Odor identification declined most rapidly in older individuals (0.25 greater decline in number correct per decade of age, P<0.001) and in men of all ages (0.32 fewer correct after 5 years vs. only 0.15 fewer correct for women; P=0.005). Blacks and Whites declined at the same rate (P=0.925), sustaining the marked cross-sectional race difference observed in Wave 1 (equal to 9 years of aging). Neither cognition, SES, health conditions, mental health, alcohol nor smoking predicted accelerated olfactory decline (all P's>0.05). In addition to having poor olfactory function, men and older people experience accelerated olfactory decline, effects not explained by our measured psychosocial or health conditions. We find no evidence of accelerated olfactory aging explaining the health disparity in Blacks seen at the Wave 1 and 2 time points, suggesting that major insults to the olfactory system occur before middle age. Acknowledgements: The National Institute on Aging (R37 AG030481 AG036762 AG029795), the Institute for Translational Medicine at The University of Chicago (KL2RR025000), the McHugh Otolaryngology Research Fund, and the American Geriatrics Society.

#P148 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Receptor Representations of Perceptual Similarity

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In the current consensus model of the olfactory code, the recognition of an odorant molecule depends on which receptors are activated and to what extent. Here we set out to determine if the receptor-activation profile for a set of camphoraceous odorants is more representative of the structural features or the perceptual similarity. The camphoraceous odor class is unusual in that despite their common perceptual odor character the odorants do not share a common functional group (median Tanimoto similarity = 0.14). Using a set of odorants described as having a camphoraceous quality (Amoore, 1970), we tested the similarity of the odorants in terms of molecular structure, receptor activation profile in a heterologous assay, and human perceptual ratings. Molecular structure was quantified using physicochemical descriptors (Haddad et al., 2008). To measure receptor-activation profiles, we cloned receptors representing 384 of the most frequent variants in the 1000 genomes data set. We then tested the odorants against these receptors using a heterologous luciferase assay. Human perceptual similarity was assayed using an air-dilution olfactometer to obtain pairwise similarity ratings. Preliminary results suggest that the receptor array is more representative of structural features than of perceptual similarity. Acknowledgements: R03-DC011373

#P149 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Taste-evoked Chorda Tympani Responses in C57BL/6J Mice Vary Depending on Which Region of the Tongue is Stimulated

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It is known that each taste bud is responsive to stimuli representing all of the basic taste qualities. However, there is also evidence that the transduction mechanisms that mediate such responses vary depending on location in the oral cavity, and the gustatory nerves differ in amiloride-sensitivity and other properties. Although the peripheral taste-responsive nerves have often been compared with each other, there have been few attempts to consider whether the properties of a particular nerve vary depending on which oral regions are stimulated with taste solutions. We therefore measured taste-evoked chorda tympani (CT) responses in mice while flowing solutions over the anterior or posterior tongue separately. Subjects were C57BL/6J mice, which were anesthetized prior to surgery to expose the CT. A silicone rubber ring was used to divide the tongue into anterior and posterior halves, and tastants were flowed selectively over one half at a time while measuring whole-nerve CT activity. Responses to NaCl and sucrose were significantly larger, but responses to HCl and quinine were smaller, when stimulating the anterior tongue relative to the posterior. The responses to NaCl mixed with amiloride, however, were similar for the two regions due to a greater suppressive effect of amiloride on the anterior as compared to posterior tongue. Our data suggest that the properties of CT fibers vary depending on the location of the taste buds that they innervate. The characteristics of our posterior tongue responses, in fact, were more similar to those normally associated with the glossopharyngeal nerve than with the CT. Additional work will be needed to delineate the relative contributions of fungiform and foliate papillae to our posterior tongue responses.

#P150 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Dried-bonito *dashi*: Taste qualities evaluated using CTA methods in wild type and T1R1 KO mice.

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Dried-bonito *dashi*, a broth used to increase the palatability of Japanese cuisine, is made from dried kelp, fish oils, shiitake mushrooms, and other sources. Flavor enhancement is due to olfactory and taste stimuli such as lactic acid, L-amino acids (including glutamate), and inositol monophosphate (IMP). Kawasaki et al. (2008) and Kondoh et al. (2012) report that rats and mice prefer *dashi* in 2-bottle preference tests. We conducted conditioned taste aversion (CTA) experiments to determine what

taste qualities mice can identify in *dashi* and if an L-amino acid receptor (T1R1) contributes to these sensations. C57BL/6J wild type (WT) mice and T1R1 knockout (KO) mice made against a mixed background and backcrossed to C57BL mice (Zhao et al., 2003) were used to see if a CTA to *dashi* generalized to (1) 5 basic tastes, and (2) individual L-amino acids (+IMP, pH 5.7-5.8) found in *dashi* (Ajinomoto, Japan), with or without lactic acid added. The role of odor cues was minimized by constant exposure to the odor of *dashi* throughout the experiment and by compromising the nasal epithelium with ZnSO4 (verified by a "chip" odor test). Generalization of the CTA was greatest to sucrose and weakest to NaCl in WT mice. WT mice also generalized this CTA to individual amino acids to a degree roughly related to the concentration of the amino acid in *dashi*. Lactic acid (1%) altered generalization of the CTA to a subset of amino acids. KO mice showed a similar pattern of generalization to basic tastes but none to L-glutamate. Even though KO mice readily learned a CTA for *dashi*, they showed minimum generalization to the other L-amino acids. These results show that *dashi* elicits a complex taste and that the T1R1 receptor contributes significantly but not entirely to that complexity. Acknowledgements: NSF IOS-0951016

#P151 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

GABA as afferent taste neurotransmitter

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ATP is recognized as a principal taste transmitter, activating P2X2 and P2X3 purinoceptors located on afferent sensory fibers that innervate taste buds. Taste buds also contain and release several other neurotransmitters. Many of these have been shown to mediate cell-to-cell communication within the bud. For instance, we recently reported that GABA serves as an inhibitory transmitter, decreasing taste-evoked ATP release from taste buds. We now ask whether GABA might also act on afferent sensory axons that innervate taste buds. To answer this question, we analyzed GABA receptors in geniculate ganglia. Neurons in this ganglion innervate fungiform and palatal taste buds. Using RT-PCR, we show that GABA-A α 1 is prominently expressed along with lower levels of α2, β2, β3, γ1 and γ2 subunits. The cation-chloride cotransporters, KCC3 and KCC4, and particularly, NKCC1, which is essential for the inhibitory action of GABA, are also expressed in geniculate ganglia. Immunostaining shows that a majority of geniculate ganglion neurons express variable levels of GABAA-α1 in their somata. Fibers projecting *peripherally* from geniculate ganglia were strongly immunopositive for GABA-α1, a pattern very similar between GABAA-α1 and P2X2. In summary, GABA may function for both cell-to-cell communications within taste buds and in afferent taste neurotransmission. Functional imaging studies are in progress to test whether inhibitory responses to GABA are detected in all or a subset of geniculate ganglion neurons. Acknowledgements: NIH/NIDCD R01DC6308 and NIH/NIDCD R21DC12746

#P152 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Expression and Signaling of IL-10 in Taste Cells

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Aged taste cells in taste buds are continuously replaced by young cells differentiated from basal cells. However, the related mechanisms that regulate survival and death of taste cells remain largely unknown. Here we continue to study the roles of cytokines tumor necrosis factor (TNF) and interleukin-10 (IL-10), in taste cell turnover. TNF, a proinflammatory cytokine, often induces apoptosis by binding to its receptors and activating cell death pathways. In contrast, IL-10, an anti-inflammatory cytokine, suppresses TNF expression and promotes cell growth and survival. We previously found that $T1R3^+$ type II taste cells are TNF-producing cells, and TNF receptors are globally expressed in taste buds. Here we report the expression and signaling of IL-10 in taste buds. We find that IL-10 and its receptor IL10R1 are preferentially expressed by different subsets of type II taste cells. Based on immuno-colocalization experiments using taste cell-type markers, the IL-10-producing cells are predominantly type II taste cells expressing the G-protein α-gustducin, while IL10R1 is selectively present in taste cells that express T1R3 and TNF. The IL-10 production can be induced by microbial products lipopolysaccharide (LPS) and Staphylococcal Enterotoxin A (SEA). The LPS-induced IL-10 expression in taste cells was profoundly diminished in *TLR2-TLR4* double-gene-knockout mice, which indicates the dependence of IL-10 induction on TLR signaling pathways. The results strongly suggest that IL-10 produced by α-gustducin+ type II cells could specifically down-regulate TNF production by acting on IL10R in T1R3+TNF+ type II cells. This interaction between the two subsets of taste cells may provide a mechanism for cellular crosstalk in taste buds under circumstances such as injury, infection and inflammation. Acknowledgements: The study was supported by NIH/NIDCD grants DC010012 and DC011735 and NSF grant DBJ-0216310

#P153 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Bitter Taste Stimuli trigger functionally distinct and interdependent Gustatory Signaling Pathways in immortalized Human Taste Cells

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Stably proliferating human taste cell lines are a powerful tool to gain new insights into human taste reception and signal transduction mechanisms. We previously established human taste cell lines from lingual epithelium, which maintain their endogenous programming and dedication to bitter taste reception. HTC-8 cells express 15 of 25 human TAS2R bitter taste receptor genes and respond to various bitter stimuli with endogenous gustatory signaling including calcium signaling and cell membrane depolarization. We used Fluo-4 calcium imaging assays and FLIPR fluorescent membrane potential assays to measure responses of human taste cells to various bitter taste stimuli and combinations of bitter taste stimuli. Our results revealed that stimulation with salicin elicits a PLC-dependent increase of intracellular calcium from internal calcium stores and does not lead to membrane depolarization. In contrast, addition of other bitter taste stimuli for instance PTC, saccharin and aristolochic acid led to cell membrane depolarization as well as to PLC-independent increase of intracellular calcium, which depends on extracellular calcium. These results suggest that gustatory responses to bitter stimuli are not uniform in human taste cells and that bitter taste stimuli may trigger distinct signaling pathways. To test, whether these distinct signaling pathways interact we stimulated HTC-8 cells with salicin in combination with PTC, saccharin or aristolochic acid in the absence of extracellular calcium. Surprisingly, even though PTC, sacharin and aristolochic acid alone elicited no response, the PLC-dependent increase of intracellular calcium in response to salicin was strongly enhanced. These results suggest that cross-talk between bitter taste receptors and/or signaling pathways may occur in human taste cells. Acknowledgements: The research was funded by BRAIN AG corporate funds.

#P154 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Sodium-sensing cells in mouse vallate taste buds

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Taste buds contain two types of cells that directly participate in gustatory transduction-- Receptor (Type II) and Presynaptic (Type III) cells. Receptor cells respond to sweet, bitter and umami taste stimulation. Presynaptic cells have been identified as sour (acid) taste-sensing cells. Using confocal Ca^{2+} imaging in a lingual slice preparation, Tomchik et al. (2007) showed that some vallate taste cells responded to salt (Na^+) taste. Recently, ion channels (ENaCs) believed to underlie salt taste transduction were reported to be in taste cells that were neither Receptor (Type II) nor Presynaptic (Type III) cells. Yet, mechanisms of Na^+ taste transduction and the identity of the cells that respond to Na^+ stimulation remain controversial. Using Ca^{2+} imaging on isolated mouse vallate taste cells loaded with Fura 2, we demonstrate here that a subset of cells, neither Receptor nor Presynaptic cells, show Ca^{2+} mobilization in response to Na^+ stimulation. Removing extracellular Ca^{2+} had no effect on responses evoked by Na^+ stimulation. In marked contrast, applying 1 μM thapsigargin, a SER Ca-ATPase inhibitor, or 10 μM U73122, a PLC blocker, eliminated Na^+ responses, suggesting that Na^+ stimulation triggers PLC/IP3-mediated release of Ca^{2+} from intracellular stores. Next, we used CHO cells expressing P2X receptors as biosensors to monitor ATP release from taste buds and isolated taste cells. Na^+ stimulation elicited robust biosensor responses that were blocked by suramin, confirming that Na^+ stimulation elicits ATP secretion from taste buds/cells. Carbenoxolone (5 μM) or probenecid (250 μM), blockers of pannexin1 hemichannels, reversibly blocked Na^+-evoked ATP secretion. Our data indicate that salt taste stimulus triggers a dedicated population of taste cells to secrete ATP via pannexin1hemmichannels. Acknowledgements: Supported by NIH/NIDCD 5R01DC007630 (SDR).

#P155 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

IL-1β Enhances Sodium Transport in Taste Buds

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Sodium ions pass through apical epithelial sodium channels (ENaC) in taste cells, depolarizing them and transmitting information about sodium taste to the brain. Salt taste transduction is among the least understood of the taste transduction pathways. Moreover, few ENaC modulators have been identified in taste receptor cells compared to epithelial cells from kidney, lung and colon. Interleukin (IL)-1β is a classical proinflammatory cytokine produced by activated leukocytes. IL-1β and its receptor are also strongly expressed in taste cells. This cytokine promotes the maintenance of normal sodium taste function after contralateral chorda tympani injury, but the direct effects of IL-1β on sodium transport in taste buds are unknown. We loaded rat lingual epithelia containing fungiform taste buds with the sodium indicator dye CoroNa Green, and measured changes in fluorescence (F_{490}) in response to basolateral IL-1β. Apical administration of the ENaC blocker, amiloride (50 μM in control Ringer's solution), decreased F_{490} by 10-15%. Basolateral IL-1β (0.05 ng/ml – 5 ng/ml in control Ringer's solution) caused upsurges in F_{490} resulting in an overall 2-10% increase in sodium transport above baseline. The effects of IL-1β were at least partially amiloride-sensitive, and occurred within seconds.

These results indicate that IL-1β rapidly augments ENaC function, in contrast to the cytokine's delayed inhibition of sodium transport in other epithelial cells. Together, this indicates a novel, direct influence of IL-1β on ENaC in taste buds, mediated by mechanisms which diverge from those acting in other sodium-transporting epithelia. Acknowledgements: NIDCD 005811-10

#P156 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Ligand Specificity of Orphan G Protein-coupled Receptor GPR84

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Previous studies concluded that medium chain fatty acids with carbon chain lengths of 9-14 were ligands for GPR84 (Venkataraman and Kuo *Immunol Lett* 101:144, 2005; Wang et al. *J Biol Chem* 281:34457, 2006), however, there has never been a careful and systematic analysis of the ligand specificity of this receptor which we have shown previously to be expressed in mammalian taste cells. As a means to compare the specificity and concentration-response functions for fatty acids in the taste system with GPR84, fura-2 based ratiometric calcium imaging was used to characterize GPR84 in a cell line that has been designed to express this receptor in an inducible fashion under control by the tetracycline (TET) promoter. The specific cell line has an inducible GPR84 + Gqi9 (a chimeric G protein; (Wang et al., 2006)), which has been cloned, validated by PCR/qPCR and verified for function in FLIPR-based calcium assays. Non-induced cells were used as controls. Using fura-2 based calcium imaging, we found that caproic ($C_{6:0}$), caprylic acid ($C_{8:0}$), capric acid ($C_{10:0}$), undecanoic acid ($C_{11:0}$), lauric acid ($C_{12:0}$), oleic acid ($C_{18:1}$), and arachidic acid ($C_{20:0}$) can all elicited a robust and reversible increase in intracellular calcium in the cells induced to express GPR84, while they cannot induce any calcium signal in the non-induced cells. Our results suggest GPR84 functions as a receptor for unsaturated fatty acids from $C_{6:0}$–$C_{12:0}$ and other fatty acids (oleic acid, arachidic acid) previously not thought to activate this receptor. Currently, we are investigating the concentration-response functions for ligands of GPR84 in the inducible cell line. The specific signaling pathway for fatty acid transduction through GPR84 receptors and its role in the peripheral gustatory system remain to be elucidated.

#P157 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Ryanodine receptors selectively interact with L type calcium channels in mouse taste cells

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We reported that ryanodine receptors, specifically ryanodine receptor type 1, are expressed in two different types of mammalian peripheral taste receptor cells: Type II and Type III cells. In Type II cells that lack voltage-gated calcium channels (VGCCs) and chemical synapses, the ryanodine receptors contributed to the taste-evoked calcium signals that are initiated by opening inositol trisphosphate receptors located on internal calcium stores. In Type III cells that do have VGCCs and chemical synapses, ryanodine rreceptors were no longer able to contribute to taste-evoked calcium release signals but contributed to the depolarization-dependent calcium influx. The goal of this study was to better understand the role of the ryanodine rreceptors in Type III cells. Specifically, we wished to establish if there was selectivity in the type of VGCC that was associated with the ryanodine receptor or if the ryanodine receptor opened irrespective of the calcium channels involved. We also wished to determine if the ryanodine receptors and VGCCs required a physical linkage to interact or were simply functionally associated with each other. Using calcium imaging and pharmacological inhibitors on a transgenic mouse line that expresses green fluorescent protein (GFP) in GAD67 expressing Type III taste cells, we found that ryanodine receptors are selectively associated with L type VGCCs but not through a physical linkage. Taste cells are able to undergo calcium induced calcium release through ryanodine receptors to increase the initial calcium influx signal and provide a larger calcium response than would otherwise occur when L type channels are activated. Acknowledgements: This work was supported by NSF Grant 0917893 to KFM.

#P158 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Functional Profile of the Adult Glossopharyngeal Nerve Following Neonatal Chorda Tympani Transection in Rats

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Rats receiving bilateral neonatal chorda tympani transection (neoCTX) show an increased preference for ammonium chloride (NH_4Cl) as adults – a substance which normal adult rats never prefer. It is currently unclear what changes to the taste system underlie this altered preference. To determine if injury-induced differences in the response properties of the remaining taste nerves can account for this behavior, whole-nerve electrophysiology was performed on the glossopharyngeal nerve

(GL) of adult rats that underwent either unilateral neoCTX or a control surgery at five days of age. Nerve activity following application of various concentrations of NH_4Cl, NaCl, and sucrose was recorded using 0.5M NH_4Cl and 0.5M KCl as standards. There were no differences in nerve response to NH_4Cl or NaCl, but there was a significant difference for sucrose, with neoCTX rats having higher GL responses to the tastant. Since NH_4Cl responses did not differ between surgical groups, there may be differences following neoCTX in greater superficial petrosal or superior laryngeal nerve activity, or alterations in central processing which can account for the increase in NH_4Cl preference. Alternatively, the functioning of the GL may be more affected following bilateral compared to unilateral neoCTX. The mechanisms which lead to the observed injury-induced alteration in sucrose responding are unknown. However, this increase in responding following neoCTX could help explain observations from the human literature in which early chorda tympani damage is correlated with an increased preference for sugary foods. Work is currently underway to record GL responses from adult rats receiving bilateral neoCTX at 10 days of age.

#P159 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Mouse bitter taste

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Depending on dose, bitter chemicals can be toxic or healthy. Accordingly, consumers like some bitter tasting foods while they avoid others. For a detailed understanding of bitter taste physiology we examined the receptors for bitter substances and their cells in mice. Functional expression analysis showed that mice and humans detect a similar range of bitter compounds even though mice possess 30% more *Tas2r* bitter taste receptor genes than humans. Intriguingly, recognition of bitter chemicals in the two species is mostly evoked by non-orthologous Tas2rs. Based on the number of cognate compounds, mouse Tas2rs, like their human counterparts, can be classified in generalists, moderately tuned receptors and specialists. However, compared with humans, mice seem to possess a larger fraction of specialists suggesting that a greater number of *Tas2r* genes offers the luxury of a set of specific receptors for selected bitter compounds. Genetic labeling and in situ hybridization experiments revealed that mice possess 2200 to 3300 bitter-sensing cells. They express the entire repertoire of Tas2r genes at individual levels and in limited subsets. Accordingly, genetic ablation of the cells expressing one Tas2r, i.e., Tas2r131, did not extinguish the entire population of bitter sensing cells but only ~50%. The remaining bitter sensing cells displayed complete absence of some Tas2rs, whereas expression of others was reduced to different extents. Behavioral experiments showed that these mice exhibit diminished avoidance of several bitter compounds, whereas they are indistinguishable from control mice in their avoidance of denatonium benzoate. Together the data demonstrate that bitter sensing cells are functionally polymorphic forming the basis for variable behavioral responses to different bitter chemicals.

#P160 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Behavioral responses to trimethylamine -*N*-oxide using the CTA paradigm in C57BL/6 mice

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Trimethylamine-*N*-oxide (TMAO) is a common and compatible osmolyte in tissues of marine organisms, and counteracts the effects of protein destabilizing agents such as urea in elasmobranches. Gadoid fish, elasmobranches and scallop have high levels of TMAO in their muscles. TMAO is thought to contribute to the taste of these fishes but the taste of TMAO is unclear. In this study, we investigated taste quality perception of TMAO in C57BL/6 mice using conditioned taste aversion (CTA) experiments.We developed LiCl-induced CTA to 1.0% TMAO and examined its generalization to 12 taste stimuli. CTA to TMAO significantly generalized to D-phenylalanine, saccharine and quinine. These results suggest that mice avoid the taste of TMAO and its taste perception in mice is similar to D-phenylalanine, saccharin and quinine. We will also present behavioral thresholds and behavioral response to low concentration (below 0.1%) of TMAO.

#P161 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Purification, biophysical characterization and first crystallization trials of the ligand-binding domain of the human T1R3 sweet taste receptor.

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The heterodimeric T1R2/T1R3 sweet taste receptor is composed of two class C G-protein coupled receptors (GPCRs), while T1R1/T1R3 heterodimer is involved in umami taste perception. Class C GPCRs share common structural homologies including a large N-terminal domain (NTD) linked to the seven transmembrane domain by a cysteine rich region. T1R2- and T1R1-NTDs have been shown to contain the primary binding site for most of the sweet ligands and umami tastants, respectively. In contrast, the contribution of T1R3-NTD to sweet and umami compound detection is less documented. The human T1R3-NTD was produced in *Escherichia coli* using a strategy recently described (Maîtrepierre *et al.*, *Protein Expr. Purif.*, 2011).

The purified protein was characterized by SDS–PAGE, circular dichroism and a fluorescent ligand-binding assay. Using size exclusion chromatography coupled to static light scattering, we showed that hT1R3-NTD is monodisperse and forms homodimers. These data demonstrate that the purified protein is not only suitable for functional analyses, but also for subsequent crystallization trials. Acknowledgements: This work was supported by fundings from INRA, Burgundy council (Région Bourgogne) and Agence Nationale de la Recherche (ANR-09-ALIA-010).

#P162 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Regulation of basal sweet sensitivity of mice by leptin.

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Leptin (Lep) is shown to selectively suppress sweet taste responses in lean mice but not in Lep receptor-deficient *db/db* mice. In contrast, endocannabinoids (EDs) enhance sweet taste sensitivities in lean mice but not in mice genetically lacking CB_1 receptors. However the action of endogenous Lep and EDs on taste responses is not fully understood. In this study, we examined expression of related molecules, the effect of leptin on taste cell responses and the effect of antagonists for Ob-Rb (leptin L39A/D40A/F41A : LA) and CB_1 (AM251) on the chorda tympani (CT) responses in mice with different serum Lep levels. About 40 % of taste cells expressing T1r3 coexpressed Ob-Rb and a subset of taste cells expressed biosynthesizing enzyme (DAGL) and degrading enzyme (MAGL) of ED (2-AG). In about half of sweet sensitive taste cells, bath application of 20 ng/ml leptin suppressed responses to sweeteners (<80% of control response). The effect of leptin was concentration dependent and reached maximal level at 10-20 ng/ml. When the cells were adapted to several concentrations (1-5 ng/ml) of leptin, increases in 10 ng/ml leptin still affected sweet responses of taste cells. Administration of LA significantly increased CT responses to sweeteners in lean mice, whereas administration of AM251 did not affect. Moreover the effect of LA on CT responses to sweeteners gradually decreased with increasing plasma leptin levels, whereas the reverse is true for ECs. These results suggest a possibility that circulating Lep may act as a modulator in mice that tonically influence basal sweet sensitivity, while ECs may become more effective with defects in Lep system. Acknowledgements: Supported by JSPS KAKENHI Grant Number 18077004, 18109013, 23249081 (YN) and 21791808, 23689076 (RY).

#P163 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Transcriptome analysis of individual taste receptor cells

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Although many genes important for taste receptor cell functioning have been identified, including *Tas1r* and *Tas2r* taste receptors and downstream signaling components *a-gustducin* and *Trpm5*, much remains unknown about these cells. In this study, we have taken a whole genome transcriptomics approach to identify genes selectively expressed in individual mouse taste receptor cells of specific varying subtypes. We standardized methods for isolating single taste receptor cells and linearly amplifying their mRNA population using a T7-OligodT primed method. Transcriptome profiling was done by deep sequencing using the illumina HiSeq platform and Affymetrix microarrays. Statistical analysis of each individual taste cell's transcriptome data from fifteen *Tas1R3* expressing type II cells, seventeen NaCl responsive type III cells, eight NaCl unresponsive type II cells and five Lgr5 expressing stem/progenitor cells demonstrates that these cell types form distinct groups. Further, many marker genes specific to each particular taste cell type are differentially expressed several thousand-fold to several million-fold, confirming the reliability of our method. We are using this method to identify pathways unique to each type of mature taste receptor cell as well as to stem/precursor cells. We are using data-mining to discover hitherto unknown functionalities of taste cells. Our method also can be applied to other cell types as well. Acknowledgements: NIH-NIDCD Core Grant 1P30DC011735-02 to Monell, NIH-DC03155 to RFM and NIH-R01DC010842, Commonwealth of Pennsylvania Department of Health to PJ

#P164 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

The L-Glutamate Chemoreceptor of *Paramecium*, an Ortholog of NMDA-like Receptor, is located in the Soma and Ciliary membranes

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Paramecium tetraurelia is strongly attracted to L-glutamate. The cells rapidly hyperpolarize in L-glutamate from a K conductance (Preston and Usherwood, 1988), causing smooth and rapid swimming and attraction to the stimulus. Upon binding to its receptor, L-glutamate initiates a rapid increase in intracellular cyclic AMP (Yang et al., 1997). Downstream from this second messenger is the activation of Protein Kinase A, that activates the plasma membrane calcium pumps to sustain

the hyperpolarizing conductance and sustain the smooth fast swimming. We have used RNA interference (RNAi) to test several candidate genes for possible function as an L-glutamate receptor and found a gene with sequence homology to the glutamate binding subunit of an NMDA-like receptor. When the mRNA for this gene, *pGluR1*, is depleted using RNAi, the cells are not attracted to L-glutamate, but continue to be attracted to D-glutamate. To better understand the signaling pathway for L-glutamate, we have epitope tagged the pGluR1 protein and found by Western blotting and mass spectrometry that it is in the membrane of the cell body and cilia. A catalytic subunit of the ciliary adenylyl-cyclase labeled with GFP does not co-immuniprecipitate with FLAG-pGluR1. Mammalian NMDA-like receptors are dependent upon glycine and D-serine, but the *P. tetraurelia* chemoresponse to L-glutamate is unaffected by combinations of glycine and D-serine and L-glutamate. Acknowledgements: NIH Grant Number 2 P20 RR016435-06 to the Neuroscience Center of Research Excellence (COBRE to R. Parsons, PI) for imaging support and NIH grant RO1 GM59988

#P165 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

A selective P2X3, P2X2/3 receptor antagonist abolishes responses to all taste stimuli in mice

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ATP is believed to be a crucial neurotransmitter for communicating gustatory information to nerve fibers. Evidence is based largely on recordings from mice lacking both P2X2 and P2X3 purinergic receptor subunits (P2X2-P2X3 DKO mice), which lack responses to all taste stimuli (Finger et al., 2005). These data suggest that all taste qualities require ATP to communicate with nerve fibers. However, subsequent studies have detected ATP release only from Type II taste cells, those that respond to bitter, sweet, and umami stimuli (Huang et al., 2007; Romanov et al., 2007). Recent experiments on the P2X2-P2X3 DKO mice have shown that in addition to the lack of postsynaptic receptors, these mice fail to release ATP to taste stimuli (Huang et al., 2011). Thus, the lack of taste responses may be due to the lack of ATP release rather than the lack of postsynaptic receptors. To resolve whether postsynaptic P2X receptors are required for transmission of all tastes to the nervous system, we have used a pharmacological approach to chemically block the purinergic receptors while recording from the chorda tympani nerve in response to a battery of taste stimuli. C57Bl6 mice were injected ip with 6 mg/kg AF-353, a membrane permeant compound that blocks all P2X3-containing receptors (P2X3 homotrimers and P2X2/3 heterotrimers; Gever et al., 2010). Within 15 min of injection, integrated responses to all taste stimuli, including acids and salts, were abolished. Taste responses also are blocked in a dose-dependent fashion with application of higher concentrations of AF-353 directly to the tongue and can be partially recovered upon washout of the drug. These data clearly indicate that activation of P2X receptors and therefore ATP release is required for all taste modalities in mice. Acknowledgements: Funded by NIH grants R01 DC012555, R01 DC007495, and P30 DC04657 and a gift from Afferent Pharmaceuticals.

#P166 **POSTER SESSION III: TRIGEMINAL; HUMAN OLFACTORY PSYCHOPHYSICS; TASTE PERIPHERY**

Nonsynaptic Contacts in Rat Circumvallate Taste Buds: Subsurface Cisternae and Atypical Mitochondria

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It is generally accepted that Type II cells transduce bitter, sweet, and umami stimuli in rodent taste buds. Recent studies also demonstrate that Type II taste cells release ATP, a neurotransmitter believed to play an important role in taste transduction. However, no classical synapses have been found to be associated with Type II cells. Are there other contacts between Type II cells and Type III cells or Type II cells and nerve processes? In the present study, we utilized conventional transmission electron microscopy to examine the ultastructural features of nonsynaptic contacts in rat circumvallate taste buds. Our results indicate that Type II cells are in intimate contact with Type III cells in taste buds. Two types of nonsynaptic contacts, subsurface cisternae of endoplasmic reticulum and/or atypical mitochondria, have been found to be present adjacent to the cytoplasmic leaflet of Type II cells at close appositions with nerve processes. Frequently we observed subsurface cisternae of smooth or rough endoplasmic reticulum in Type II cells at sites of apposition with nerve processes. Occasionally we observed atypical mitochondria and subsurface cisternae adjacent to each other in Type II cells. We also observed electron-dense periodic pillars connecting the subsurface cisternae or the atypical mitochondria to the membranes of Type II cells at close appositions with nerve processes. We speculate that these structures are involved in communication between Type II cells and nerve processes. Acknowledgements: This work is supported by NIH grants DC00285 and P30 DC04657

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POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

A role for bitter taste receptors in thyroid toxicity and hormone production

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Bitterness is associated with toxicity. Bitter compounds activate a small family of G protein-coupled taste receptors (T2Rs) expressed in the taste buds. T2Rs are also found in non-gustatory tissues (e.g., the respiratory and gastrointestinal systems), suggesting that many ingested or inhaled toxins could have broad physiologic effects. We report that T2Rs are expressed in thyroid follicular cells (FCs), where they modulate iodide efflux. Immunohistochemical and PCR analyses show that numerous T2Rs as well as the T2R-associated G protein subunit α-gustducin are expressed in human and rodent FCs and in a human follicular cell line, Nthy-Ori 3-1. Thyroid stimulating hormone (TSH)-dependent Ca^{2+} signals, an important regulator of iodide efflux from FCs, were significantly reduced in Nthy-Ori 3-1 cells by the T2R ligands denatonium benzoate (DB), chloramphenicol (Chlor) and cycloheximide (Cyx). By contrast, the T2R38 ligand 6-n-propylthiouracil (PROP) had no effect on TSH-dependent Ca^{2+} signals, likely because this cell line expresses only the "non-taster" T2R38 variant. DB, Chlor and Cyx also significantly reduced TSH-dependent iodide efflux from Nthy-Ori 3-1 cells. Decreased iodide efflux *in vivo* should result in decreased production of the thyroid hormones triiodothyronine (T3) and thyroxine (T4). Consistent with this, we found that a nonsynonymous polymorphism in T2R42 is associated with lower free T3 and T4 levels in a human cohort. Thyroid hormones can affect energy expenditure, thermoregulation, body weight, and body composition. T2Rs may be a useful target for pharmacologic regulation of these endocrine signals, perhaps leading to new interventions for chronic morbidities involving fatigue or obesity. Acknowledgements: Support: NIDCD (R01 DC010110), NIDDK (P30 DK072488).

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POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Metabolic effects of long-term sweetener consumption

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The sweet taste receptor T1R2+T1R3 responds to diverse gustatory stimuli including sugars and low calorie sweeteners (LCS). In intestinal enteroendocrine L cells, T1R2+T1R3 couples glucose stimulation to the secretion of insulinotropic hormone glucagon-like peptide-1 (GLP-1). While the preponderance of in vivo evidence indicates that LCS do not impact glucose homeostasis, the responsiveness of T1R2+T1R3 to natural and artificial LCS suggests that these compounds could exert extraoral effects. To address this issue, we have initiated long-term sweetener (300 mM sucrose, Su; 1 mM sucralose, Sa; 10 mM cyclamate, Cy; 3 mM acesulfame K; 5 mM rebaudioside A) consumption studies in mice with ($T1R3^{+/+}$) or without ($T1R3^{-/-}$) a functional sweet taste receptor. Mice (4 w.o.) are maintained for 3, 6, 9 or 12 mo. on normal chow diets along with ad lib water containing one of the sweeteners. Cy serves as a negative control as it is not an agonist for mouse T1R2+T1R3. Mice are assessed for food and fluid intake, sweet taste preference, body weight, body fat, metrics of glucose and insulin homeostasis, and glucose-stimulated GLP-1 secretion from ileum and colon explants. Initial results indicate that both $T1R3^{+/+}$ and $^{-/-}$ mice maintained on 300mM Su have significantly higher body fat content than either Sa- or Cy-treated mice. By contrast, Sa-treated mice show a strong potentiation of glucose-stimulated GLP-1 secretion (as compared to Su- or Cy-treated mice) at 3 mo, with reduced potentiation at later time points. Interestingly, glucose tolerance tests revealed no significant differences in glucose or insulin levels across these sweetener groups. Ongoing assessments of all five sweeteners will be presented. Acknowledgements: Tate&Lyle and NIDCD (DC010110)

#P169 POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Oral stimulation with sugar elicits cephalic phase insulin release and improves glucose tolerance in C57BL/6 and *Tas1r3* knock-out mice

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In rats, oral stimulation by sugars elicits cephalic phase insulin release (CPIR). This CPIR has been found to improve tolerance to glucose challenges. Here, we asked whether oral stimulation by glucose has similar effects in C57BL/6 wild-type (WT) mice. To explore the role of the T1r3 subunit of the heterodimeric sweet taste receptor (T1r2+T1r3) in this process, we also examined *Tas1r3* knock-out (KO) mice. We subjected all mice to a 2 g/kg glucose challenge. To this end, we administered a 2.8 M glucose solution either orally (by allowing mice to take a predetermined number of licks) or post-orally (by injecting a specific volume into the esophagus by feeding tube). We collected tail blood immediately prior to glucose administration (at 0 min), and at subsequent time intervals. In Experiment 1, we measured plasma insulin levels with an ELISA test. We inferred a CPIR if plasma insulin increased significantly between the 0 and 5 min measurements. Both strains of mice exhibited a significant CPIR after oral stimulation, but not after post-oral stimulation with glucose. The fact that both strains exhibited a CPIR of similar magnitude indicates that T1r3 is not necessary for eliciting the CPIR. In Experiment 2, we measured blood glucose levels at 0, 15, 30, 60 and 120 min. We found that both strains exhibited significantly better glucose tolerance when the glucose was administered orally than post-orally; the benefit of oral administration was especially pronounced in the *Tas1r3* KO mice. These results indicate that oral stimulation by sugars elicits a CPIR via a T1r3-independent taste mechanism, and that this CPIR substantially improves the ability of mice to tolerate glucose challenges. Acknowledgements: Summer Undergraduate Research Fellowship Program, Columbia University

#P170 POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

As American as Apple Pie Gum: A Study of Satiety

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Purpose: The aim of this study is to determine the satiety value of Wrigley's Extra Dessert Delight Apple Pie Sugar-Free Gum as compared to a 100 calorie slice of apple pie. **Procedure:** Thirteen girls and 11 boys self-assessed their degree of satiety on a visual analog scale before and after chewing Wrigley's Extra Dessert Delight Apple Pie Sugar-Free Gum for one, 15, and 30 minutes. This was repeated on a separate day with a 100 calorie slice of Market Pantry Apple Pie (Target) or vice-versa (the order of presentation being counter balanced). A satiety value was computed for each and statistical significance was determined for difference in satiety index between the two and effect of order of presentation (pie versus gum first). **Conclusion:** No statistically significant difference was seen in satiety value in response to eating a slice of apple pie or chewing apple pie-flavored gum (p=0.096). No effect of order presentation was seen. The gum imbued the same satiety value as apple pie, with less than 1/20 of the calories. The results suggest that chewing Wrigley's Extra Dessert Delight Apple Pie Sugar-Free Gum may have a role in the promotion of satiety in children as part of a weight loss program.

#P171 POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Pre-absorptive insulin release to glutamate taste

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Glutamate, like glucose, requires insulin to be transported out of blood into tissue. Glutamate is detected in the mouth by taste cells, in the intestine by L-cells and in the pancreas by Beta cells. In addition, glutamate stimulates glucagon release from pancreatic alpha cells. It is unknown, however, whether pre-absorptive insulin release (PIR) occurs in response to the taste of glutamate. The purpose of this study was to determine whether glutamate causes PIR and whether the magnitude of PIR was related to glutamate taste sensitivity, which is variable among individuals. To assess PIR, human subjects tasted and consumed a glutamate test meal at a dose of 100mg/kg body weight. The glutamate dose was comprised of a mixture of monosodium

glutamate and monopotassium glutamate. Subjects tasted the mixture by repeated swishing and spitting for 5 minutes. Subjects then ingested another dose of glutamate. Baseline blood samples were collected every 5 minutes before ingestion of glutamate. After ingestion, samples were collected at 3 minute intervals for a total of 15 minutes and analyzed for glucose, insulin and c-peptide. To assess glutamate sensitivity, subjects tasted and rated intensity matched NaCl, sucrose, and glutamate solutions. Relative glutamate sensitivity was defined as the ratio of perceived glutamate intensity to that of NaCl and sucrose. All seven subjects showed pre-absorptive blood glucose changes in response to the taste of glutamate. Six subjects showed increases in blood glucose (presumably due to glucagon release) and one subject showed a decrease. Half of the subjects showed pre-absorptive changes in insulin. The highest PIRs occurred in the two subjects who showed the highest sensitivity to glutamate. The lowest PIR occurred in the subject with the lowest sensitivity to glutamate. Acknowledgements: NIH DC02995

#P172 **POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION**

Mice lacking Trpm5 show reduced dietary fat intake

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We recently showed a critical role of Trpm5 in the transduction pathway for long chain polyunsaturated fatty acids (Liu et al., *J Neurosci* 31: 8634, 2011). In the present study, we have begun to investigate dietary fat preference and the propensity to develop dietary-induced obesity in mice lacking Trpm5. In male mice placed on a high fat diet, those mice lacking Trpm5 ($Trpm5^{-/-}$) ate significantly less and accordingly weighed less and had less body fat than wild type ($Trpm5^{+/+}$) mice; no differences between $Trpm5^{-/-}$ and $Trpm5^{+/+}$ mice were seen on a control (low fat) diet. Similar differences were recorded in control male mice and those lacking IP_3R_3, receptors that are upstream of Trpm5 activation in the fatty acid transduction pathway. Most surprisingly, however, was the fact that female mice with or without IP_3R_3 did not show the same differences indicating a potential gender effect of this pathway on dietary fat intake. Given these data, we have performed feeding studies on female $Trpm5^{-/-}$ and $Trpm5^{+/+}$ mice to look for similar gender-specific effects on fat intake. Like male mice, female mice lacking Trpm5 show a decrease in dietary fat intake and gain less weight than wild types, though these effects are much less robust and have a much slower onset than for the male mice. However, unlike the males, there is no significant difference in body fat between female $Trpm5^{-/-}$ and $Trpm5^{+/+}$ after being on the high fat diet for 56 days. We are currently exploring the specificity of these effects for the different classes of fat (saturated versus unsaturated). Together, our data indicate that Trpm5 may play a role, directly or indirectly, in the control of dietary fat intake and that these effects appear to be significantly influenced by gender. Acknowledgements: Supported by NIH grant R01DK059611 (TAG)

#P173 **POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION**

Human Anticipatory Blood Pressure Responses to Oral NaCl and KCl are Different

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The mechanism of association between dietary sodium and blood pressure is not clearly defined, but high dietary salt intake is considered a risk for hypertension (HTN) and cardiovascular disease (CVD). Many studies have examined the impact of different dietary cations on these risk factors and implicate sodium (or Na/K ratio) as a key determinant. We previously presented data showing an anticipatory blood pressure (BP) response to the oral presentation of 1.0 Molar NaCl and suggested this may be linked to blood volume pre-absorptive reflexes. Based on this premise, we hypothesized that this anticipatory reflex would be more pronounced for sodium ions. To determine the specificity of the response to oral sodium, subjects rinsed orally with either 0.5 M KCl (matched for taste intensity to NaCl) to test cation composition and 1.0 M Na-Gluconate to test salt taste intensity. Subjects rested in a seated position for 2.5 hours while we recorded resting BP and additional readings following the rinse at 10 minute intervals with a manual sphygmomanometer, one trial per day, five trials for each solution tested. In subjects whose blood pressure dropped following a rinse with NaCl, a similar trend was observed after a rinse with Na-Gluconate. Yet BP remained level, without a decreasing trend, following a rinse with KCl. Interestingly, the BP response to Na-Gluconate was weaker than the NaCl response, suggesting an influence of taste perception on the anticipatory BP reflex. The difference between the BP response to NaCl and to KCl suggests that there may be oral chemosensory specificity to the reflex. These data support the idea that anticipatory BP reflexes are cation specific and may involve gustatory mechanisms. Acknowledgements: Funded in part by NIH DC 02995 to PASB.

#P174 POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Odor Identification Performance in Middle Aged Obese Individuals with High Blood Pressure

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Obesity is a major health epidemic that affects people globally and is associated with the development of serious comorbidities such as diabetes, hypertension, and heart disease. The presence of obesity has also been linked to the risk for later development of Alzheimer's Disease (AD) or mild cognitive impairment (MCI) and has also been associated with poorer performance on cognitive measures of global, executive, and memory functioning. Furthermore, olfactory functioning is linked to energy balance and metabolism and has been shown to be altered in obese individuals, as well as those diagnosed with AD or MCI. It has been proposed that the impact of obesity on cognition is indirect and influenced by comorbidities such as hypertension and diabetes. Therefore, the current study sought to determine if odor identification performance differed between obese individuals with and without high blood pressure. Thirty-one obese individuals (BMI > 30 kg/m^2) between the ages of 46-54 years old were given the San Diego Odor Identification test. Obese individuals with high blood pressure performed significantly worse on the odor identification task (F= 8.384; p = .008), but neither group significantly differed in BMI or odor threshold. The results suggest that obese individuals with high blood pressure are more likely to show odor memory deficits and that these changes occur as early as during middle-age. Acknowledgements: Supported by NIH grant #AG004085-25 to CM.

#P175 POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Effect of Oral Sensations on the Relief of Thirst

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Thirst is the internal sensation of a need to drink, presumably to rehydrate or recover bodily fluid losses. But thirst is quenched long before all ingested fluids are absorbed. Therefore, sensory feedback must play a role in thirst quenching. Different beverages seem to quench thirst with different efficiencies, but how their oral sensory characteristics determine the thirst quenching efficacy is poorly understood. The purpose of this study was to determine which oral sensation(s) commonly manipulated in beverages, such as temperature or carbonation, influence levels of thirst. To answer this question, subjects who were deprived of liquid overnight were first asked to drink a fixed volume of an experimental beverage presenting one or two specific traits. Then we objectively evaluated their residual thirst by measuring how much additional plain, uncarbonated, room temperature water they wanted to drink afterwards. The results show that the perception of coldness is an important parameter for thirst quenching. A beverage at low temperature (5°C) quenches thirst more than a beverage at room temperature (20°C). Moreover, a cold, carbonated beverage relieves thirst even more than does a cold uncarbonated beverage. These results support, in part, the observations of the sensory controls of thirst quenching in the animal literature. Acknowledgements: Suntory Business Expert Ltd.

#P176 PPOSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Intraduodenal infusions of sucrose influence conditioned and unconditioned affective taste-guided responses to oral sucrose

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Sensory signals ascending from the oral cavity and viscera are integrated in the CNS to adjust meal size and taste preferences. Electrophysiological data suggest such integrations affect early processing in brainstem taste nuclei. Taste receptors (e.g. T1R) are also found in GI cells, but whether *taste-like* signals arising

from postoral sites are integrated with oral taste-guided behaviors is unknown. This study examined effects of intraduodenal (ID) infusions of a sweet ligand on conditioned and unconditioned affective responses to matching oral chemosensory stimuli. First, rats were given two separate 15 min sessions to ingest 0.3M sucrose directly followed by either ip LiCl (3 mEq/kg) to condition a sucrose taste aversion (CTA, n=9) or saline (unconditioned, n=8). Then, licking responses to 5 sucrose concentrations (0.01, 0.03, 0.1, 0.3, 1M), 0.12M NaCl, and water (10s trials in randomized blocks) were examined in two 30 min brief-access tests. Four min before each test, rats were infused ID with 0.3M sucrose or 0.15M NaCl (3ml). For unconditioned rats, ID sucrose enhanced preferential licking to 0.03-1 M oral sucrose, with no effect on licking for NaCl. This preference shift emerged rapidly by trial block 2. CTA rats reduced licking to 0.03-1M sucrose, not NaCl, but because CTA rats initiated so few trials, and significantly fewer after ID sucrose versus ID NaCl, detection of emergent differences due to ID preload type was likely limited. Thus, a taste reactivity test was conducted in a separate group of CTA rats. ID 0.3M sucrose preload (n=6) significantly increased gaping to intraoral 0.3M sucrose infusions (0.5ml/30s every 3min for 15min) relative to ID 0.15M NaCl preload (n=7). Together, the results suggest postoral stimuli impact oral taste processing in chemospecific ways.
Acknowledgements: NIH-T32DC000044

#P177 **POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION**

An interaction of chronic and acute metabolic states on olfactory perception associated with ghrelin signaling

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Olfaction is key for the evaluation of food cues in the environment. It is therefore not surprising that evidence is emerging for metabolic influences in olfaction. For example, receptors for feeding-related molecules such as ghrelin are expressed within the olfactory system and olfactory sensitivity is increased in fasted vs. fed state in rodents. However, human studies have generated conflicting results. This study tested whether the influence of acute homeostatic state (fasted vs. fed) on olfactory perception could be moderated by body mass index, which is associated with chronic metabolic alterations. Twenty-one subjects (14 healthy weight/HW, BMI M=22.3 SD=1.9; 7 overweight/OW, BMI M=28.2 SD=2.8) rated the intensity of odors (chocolate, strawberry, honeysuckle and lilac) and tastes (chocolate and strawberry flavored milk) using the general labeled magnitude scale in fed and fasted states (separate counterbalanced days), concomitant to an fMRI study. Blood samples were also collected on a subset of subjects (n=15) to assess the influence of internal state on feeding-related molecules. A repeated measures ANOVA of intensity ratings revealed a 3-way interaction between state (fed vs. fasted), stimulus (odors vs. taste) and group (HW vs. OW) ($f(1,19)=7.52$, $p=.013$), where odor intensity ratings decreased significantly in fed vs. fasted for OW but not HW subjects. Critically, the difference in odor intensity ratings between fasted and fed correlated negatively with difference in ghrelin change from baseline between fasted and fed conditions ($r(13)=-.615$, $p=.016$); the smaller the change in intensity perception, the larger the change in ghrelin levels. These findings demonstrate that chronic and acute metabolic states interact to influence olfactory perception possibly through ghrelin signaling.
Acknowledgements: Supported by R01 DK085579.

#P178 **POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION**

Oral Sweet Taste Stimulation Induces Cephalic Phase Carbohydrate Oxidation in Humans

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Objective: Sensory stimuli induce many anticipatory reflexes. Specifically, oral sweet taste stimulation increases glucose absorption in rats and induces cephalic phase insulin release in animals and humans. This study aimed to investigate whether oral sweet taste stimulation also induces an acute increase of carbohydrate oxidation in humans. Methods: This was a randomized, crossover design study with two test visits delivering: 1) control (DI water) and 2) 10% sucrose (w/w) solutions orally. An indirect hood calorimeter was used to measure energy expenditure (EE) and respiratory quotient (RQ) through gaseous exchanges. Each measurement was performed at one to two hours after habitual breakfast or lunch, where participants were instructed to consume an identical meal at identical times before their visits. Calorimeter measurement was preceded by a 30-minute habituation period, followed by oral stimulation and subsequent measurement for 30 minutes. Changes in EE and RQ were tested using a general linear model for repeated measures ANOVA in SPSS. Results: Nine participants have completed the study (8 females and 1 male, mean age=25.2 ± 4.6 years, mean weight=59.2 ± 4.3kg, mean BMI=21.6 ± 2.5kgm^{-2}). Energy expenditure following test solution stimulation did not change and was not significantly different between solutions (time and interaction effects, $P>0.05$). However, RQ was significantly increased after sweet taste stimulation (time effects, $p<0.001$; interaction effects, $p=0.018$), which occurred mainly during the first 10 minutes after exposure. Conclusions: Oral sweet taste stimulation increased carbohydrate oxidation in humans. The specificity of the response remains to be determined.

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POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Energy supply in chemosensory cilia of olfactory receptor neurons: Possible role of glycolysis

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The chemosensory cilia of olfactory sensory neurons are long and thin structures (~ 60 x 0.2 µm) devoid of inner membranes, specialized in odorant transduction. A cAMP pathway couples the activation of odor receptors with the opening of cyclic nucleotide-gated channels. During the odor response, the cilia undergo high levels of ATP hydrolysis, as this nucleotide is used by adenylyl cyclase, ATPases and kinases. Our estimates of resting ATP level, ATP diffusion and consumption suggest that the mitochondria, located near the base of the cilia, are insufficient to sustain chemotransduction in the entire cilium under intensive stimulation. Nuñez-Parra et al (Chem Senses 36:771-7802012) found glucose transporters in the sustentacular cells of the olfactory epithelium. We hypothesize these cells release glucose to the mucus, the cilia incorporated it from there and utilize it by glycolysis, supplementing the required ATP. To test this idea, we detected glycolytic enzymes by immunoblot of a ciliary membrane preparation. Additionally, we measured cilia and knob accumulation of a fluorescent deoxyglucose analog when applied to mucosal side of the olfactory epithelium, suggesting the apical presence of a glucose transporter. We demonstrated by immunocytochemistry the ciliary location of this transporter in isolated rat and toad olfactory neurons. Additionally, field recordings (electroolfactogram) indicated that inhibition of glycolysis and oxidative phosphorylation impairs the odor response. Altogether, these results are consistent with a dual supply of ATP in olfactory cilia, oxidative phosphorylation and glycolysis. Acknowledgements: FONDECYT 1100682 (JB), DI/VRIEA/PUCV (JGR)

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POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Dietary calcium intake and ethnicity may contribute to individual differences in taste perception.

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Calcium status affects preferences for calcium and sweet solutions in rats and mice: calcium deficient rodents drink more calcium solutions and avoid sweet compounds. Moreover, preference for calcium is inversely correlated with preference for sweet compounds in calcium replete mice. However, little is known about the relationships between calcium status and taste perception in humans. Here we measured detection thresholds for $CaCl_2$ and sucrose, and assessed intensity and taste quality ratings of $CaCl_2$, sucrose, NaCl, QHCl and citric acid in an ethnically diverse group of people in relation to dietary calcium intake. African-Americans had significantly higher detection thresholds than Caucasians for both $CaCl_2$ and sucrose. They rated 25 mM $CaCl_2$ as predominantly sour significantly more frequently than Caucasians. There was no relationship between dietary calcium intake and $CaCl_2$ detection threshold. In African-Americans but not Caucasians sucrose detection threshold was inversely correlated with dietary calcium levels (Spearman's rho = - 0.93, $p<0.001$). Dietary calcium levels also affected psychophysical ratings of NaCl and citric acid. Ethnic differences in taste perception are often explained by socioeconomic factors but there are large disparities in calcium metabolism and genetic variations in sweet taste receptor genes between African-Americans and Caucasians that may underlie the racial differences observed in our study. Our results provide new information about the relationship between calcium status and taste perception in humans; they underscore the importance of further investigation into the metabolic mechanisms responsible for ethnic differences in taste perception. Acknowledgements: Pennsylvania Health Research Formula Funds

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POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Differences in food cue reactivity between normal weight and overweight individuals?

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Overweight occurs when energy intake exceeds energy expenditure over the long term. Overweight people have been suggested to be more sensitive to rewarding effects of food (e.g. Davis et al., 2004; Franken & Muris, 2005). In the anticipatory phase of eating, odors can be considered as external cues that signal the energy content and hence the reward value of a food. In overweight individuals internal hunger signals are thought to be overruled by external food cues (Herman & Polivy, 2008). This study aims to determine if food cue reactivity is higher in overweight compared to normal weight individuals. Frequency of choice for energy-dense food items and amount of food intake reflect food cue reactivity. 25 overweight (BMI mean: 31.33 kg/m2, SD: 3.36) and 25 normal weight (BMI mean: 21.84 kg/m2, SD: 1.78) females, matched on age and restraint score, participated. In 6 separate sessions they were exposed to odors of three different categories (signaling non-food, high-energy food, low-energy food) in two motivational states (hungry and satiated). High-energy preference was measured with a computerized forced choice task and food intake (kCal) was determined with the use of a Bogus Taste Test. We hypothesize that increased food cue reactivity in overweight women is demonstrated by a stronger tendency to choose high-energy food products after being exposed to high-energy food odors, and may subsequently lead to more food intake compared to lean individuals. However, preliminary results (N=28) indicate that there is no main effect of odor on high-energy food preference (p=0.755) and also no interaction effect between odor and BMI group (p=0.935). Our first results on food intake (N=48) indicate no main effect of odor (p= 0.792) and no interaction effect of odor and BMI group (p=0.323). Acknowledgements: This study was funded by NWO (The Netherlands Organization for Scientific Research), Veni grant nr. 451-11-021, awarded to SB.

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POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Development of Viral Based Gene Delivery for Conditional Ablation of Specific Brain Peptidergic Neurons

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Learning plays a crucial role in the establishment and strengthening of food preference and we hypothesize that specific limbic system neuropeptide pathways play an important role. Identifying neural mechanisms that mediate affective aspects of taste perception will further our understanding of how the brain controls eating and overeating. We have identified two neuropeptides, corticotrophin releasing factor (CRF) and somatostatin (Sst), which are expressed in limbic system neurons that project to a hindbrain neural substrate critical for establishment of gustatory hedonic value; the pontine parabrachial nucleus. Our goal is to develop a viral construct capable of directing conditional expression of nitroreductase gene (NTR) to Sst and CRF cell populations in the limbic system of mice using a cre/lox system. Thus, specific peptide producing neurons can be rapidly ablated in isolation following treatment with the prodrug CB1954 allowing assessment of their role in central taste processing and taste-guided behaviors. In vitro cell culture of HEK293 cells combined with FLOW cytometric analysis indicate that we can conditionally express NTR and cause cell death following CB1954 treatment. Acknowledgements: This research work was supported by a grant from the Kentucky Science and Engineering Foundation as per Grant Agreement #KSEF-148-502-11-277 with the Kentucky Science and Technology Corporation.

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POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Combinatorial and genotype specific co-expression of the major urinary proteins (MUPs) during mouse postnatal development: from fundamental aspects of olfaction to innovative prospects in biomedicine

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Major urinary proteins (MUPs) of the house mouse form a large group of highly polymorphic acidic isoforms with molecular masses of 18-20 kDa. MUPs are encoded by the *Mup* gene cluster, which consists of about 35 genes and pseudogenes and is mapped to chromosome 4. Nowadays MUPs are considered as a key component of the mouse olfactory signature which can provide all essential information about the individuality of donors. There is also rapidly growing evidence that several MUP isoforms are involved in the regulation of glucose metabolism (Zhou, Rui, 2010) and can be used as sensitive biomarkers in early diagnosis of experimental nephritis (Wenderfer et al., 2009) and hepatocarcinogenesis (Ritorto, Borlak, 2011). These studies open practically unexplored biomedicine avenue for using MUPs as new protein markers which are very suitable for diagnostic purposes. We examined ontogenetic profiles of MUPs expression in male and female mice of CBA/LacY and C57BL/6JY strains using electrophoresis in polyacrylamide gel (PAGE). Quantitative evaluation of eight MUPs isoforms (A-H) revealed that each genotype is characterized by specific combinations and different proportions (ratios) of the same MUP fractions. These sex and genotype specific ratios emerged in both sexes very soon after weaning, remain quite constant in adults and resemble «barcode». Our data suggest that the pattern of *Mup* genes expression during mouse ontogenesis is regulated through a very stable genetic program. We suppose that at the early stage of illness this ontogenetic program is destroyed and the expression pattern of several *Mup* genes will be changed. These processes are reflected in the appearance of new protein profiles with altered MUPs' ratios and may correspond to epigenetically changed expression of the *Mup* gene cluster. Acknowledgements: Supported by Russian Foundation for Basic Research (projects 02-04-49273, 07-04-01762).

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POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

The Association of Taste with Adiposity in the Beaver Dam Offspring Study

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Taste sensation may influence food choice and consumption which in turn may play a role in the maintenance of health. The objective of this study was to determine the relationship between taste and changes in adiposity and related health measures during a 5 year follow-up period in the Beaver Dam Offspring Study. Whole mouth suprathreshold taste intensity was measured for salt, sweet, sour, and bitter at baseline (2005-2008) using filter paper disks and a general labeled magnitude scale. Health outcomes measured at baseline and follow-up (2010-2013) included body mass index (BMI), waist circumference, systolic and diastolic blood pressure, total cholesterol, and hemoglobin A1c (HbA1c). Cluster analysis was used to group participants according to observed patterns of intensities of the 4 tastes. In preliminary analyses (n = 1681, mean age at baseline = 48.9 years, range = 22-84 years), there were associations between patterns of taste intensities and 5-year changes in BMI, waist circumference, and HbA1c level. With adjustment for age and sex, the cluster with high intensities for all 4 tastes demonstrated a significantly greater mean increase in BMI (+ 0.96 kg/m^2) and HbA1C (+ 0.37%) than the cluster with average intensities for the 4 tastes (BMI: + 0.32 kg/m^2; HbA1c: + 0.21%). Similar results were observed for waist circumference (high intensities cluster: + 3.01 cm; average intensities cluster: + 1.87 cm). In these preliminary analyses, oral sensation, characterized using patterns of perceived intensities of suprathreshold tastes, was found to be associated with 5-year changes in some adiposity-related health outcomes. Acknowledgements: The project described was supported by R01AG021917 from the National Institute on Aging, National Eye Institute, and National Institute on Deafness and Other Communication Disorders. The content is solely the responsibility of the authors and does not necessarily reflect the official views of the National Institute on Aging or the National Institutes of Health.

#P185 POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Social Olfactory Cues and Stress

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Olfactory cues have the potential to precipitate emotional responses and thereby alter mood, judgments and behavior. In prior work, we demonstrated that exposure to a novel odor while undergoing a laboratory stressor caused individuals to re-experience stress (increased heart rate & self-reported stress) when re-exposed to that odor three days later. We wished to evaluate the potential for odor to alter stress levels following a standard laboratory stressor. One class of olfactory stimuli which has shown promise in eliciting robust effects on mood and emotion are social odors. Lundström et al. (2008) demonstrated that smelling a stranger's body odor activated a marked response in the amygdala of subjects, despite a low conscious recognition of the odor or its source. In this study, we evaluated the changes in autonomic stress levels following the Trier Social Stress Test among individuals in 3 groups who were exposed to either the body odor of their sibling, the body odor of a stranger or a non-social (fragrance) odor. Axillary odors were collected from non-twin, whole, biological siblings who were then recalled to participate in the main study in which one of the 3 odors was administered following the stress task. Results showed a significant decrease in post-recovery heart rate only among the group smelling the sibling odor, whereas skin conductance was significantly reduced for both the sibling odor and the fragrance. Following a stressor, exposure to the stranger body odor maintained arousal levels longer suggesting that both familiar and stranger body odors may be potent cues for emotional responses. Acknowledgements: Supported by the U.S. Army Research Office grant # W911NF-11-1-0087, entitled "Learning & Olfaction: Understanding and Enhancing a Critical Communication Channel".

#P186 POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Can a chemosensory threat be masked?

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The well-established angry advantage effect has been extended in recent crossmodal visual-olfactory studies using schematic human faces and human body odors. In a threat-detection task, humans detect an angry (threatening) schematic face in an array of neutral distracter faces more quickly than a friendly (non-threatening) face, hence the label 'Angry advantage'. We have previously shown that the body odor of unknown individuals (Strangers) – an established threatening olfactory stimulus – speeds a subject's detection of threatening faces, but not non-threatening faces, relative to exposure to the subject's own body odor (Self). Using event-related potential (ERPs), we have more recently demonstrated that the presence of a Strangers' body odor causes a non-threatening face to be processed as a threatening stimulus. In the present ERP study, we sought to determine whether the chemosignal mediating the aforementioned ERP effect could be masked by a common odor (Mask). Angry and neutral schematic faces were presented to subjects in the presence of Strangers' body odor + Mask, 'Self' body odor + Mask, or Mask only control, which were delivered intra-nasally by a computer-controlled olfactometer. Preliminary analyses suggest that even in the presence of an odor mask, exposure to the body odor of a stranger, relative to the odorless control and 'Self' body odor, results in significant differences in the late (cognitive) components of visual processing. This suggests that body odor can modulate the cognitive evaluation of visual stimuli even in the presence of a perceptual odor mask. The effects of masked body odor and common odor exposure on visual processing will be presented and discussed within the framework of the adaptive advantages conveyed by heightened sensitivity to threat-related stimuli. Acknowledgements: This work was supported by the National Institute on Deafness and other Communication Disorders – NIDCD (R03DC009869) awarded to JNL

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Differential responses to two kairomonal cues in mosquitoes

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Culex quinquefasciatus, Aedes aegypti, and *Anopheles gambiae* are vectors of diseases that are among the main causes of human mortality and morbidity worldwide. Host-seeking in these species is primarily regulated by olfactory cues. The most important cue for the activation of host-seeking is carbon dioxide (CO_2), the principal by-product of respiration. All three mosquito species were able to detect and follow pulsed stimuli of CO_2 at the level of olfactory receptor neurons (ORNs) housed within capitate pegs on the maxillary palps. The temporal coding capacity of *C. quinquefasciatus* CO_2-sensitive ORNs, however, was significantly lower than that of the other two species. This differential physiological response was reflected in the behavioral response to CO_2, and correlates with the CO_2 emissions from the preferred hosts for each of these species. Furthermore, aeration extracts taken from preferred hosts were analyzed by gas chromatography coupled single sensillum recording (GC-SSR) of the capitate pegs. We identified (*R*)-1-octen-3-ol, a component in human headspace volatiles, as a physiologically active in each species, although with different sensitivities. It is interesting to note that (*R*)-1-octen-3-ol was absent from bird aeration extracts. Landing bioassays using the host aeration extracts revealed behavioral responses of the three species consistent with their host selection preferences. The addition of biologically relevant concentrations of (*R*)-1- octen-3-ol to bird aeration extracts either inhibited or increased the behavioral response of the mosquitoes, consistent with its role as a non-host and host volatile, respectively. Here, we show that the host-seeking behavior of mosquitoes may be differentially regulated by olfactory signals emitted by potential hosts in their environment.

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Effects of 5a-Androst-16-EN-3a-OL Scent Administration on Augmenting Male Gambling Behavior

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The effects of pheromones on non-humans have been extensively studied. However, less is known on how such scents can elicit responses in humans. Previous research indicates that the scent of a female can affect various emotions and behaviors of males. The present study assessed the effects of Androstenol on gambling behavior in males. Participants completed an ad libitum blackjack gambling task while exposed to either no scent (control) or androstenol (experimental condition). Results indicate males gambled for a significantly longer period of time when exposed to androstenol, $t(36) = 2.09$, $p<.05$. Scores on a Sensation Seeking Scale also indicate an interaction between scent administration and personality characteristics. Thus, the administration of certain female pheromones may lead to an increased desire in males to engage in sensation seeking or risk-taking behaviors Acknowledgements: West Virginia Space Grant Undergraduate Research Fellowship

#P189 POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Earwax and Underarms; the Odd Odor Couple

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The human adenosine triphosphate (ATP)-binding cassette (ABC) transporter *ABCC11* gene encodes an ATP-driven efflux pump protein that plays an important function in ceruminous glands of the auditory canal. This protein is also expressed in apocrine sweat glands and appears to regulate the secretion of axillary odor precursors. It has been shown that a simple change in the ABCC11 gene results in different types of axillary odorant and ear wax production. Individuals who are homozygotic for a single nucleotide polymorphism (538G>A), which changes amino acid 180 in the resultant protein's polypeptide chain from glycine (G) to arginine (R), were found to have significantly less of the characteristic axillary odorants than either those who are heterozygotic for this change or those who had the wild type gene. Asian populations differ markedly from non-Asians in their ear wax type and underarm odor production. G180R SNP also is associated with a dry, white earwax phenotype that

is predominant in Asians. The G180R SNP is rare in Africans and Caucasians who typically exhibit wet, yellow earwax. For the first time, analytical analysis of earwax odorants has been performed and the principle odorants in both earwax phenotypes will be discussed. The odor of each ear wax type was informally accessed and the principal odorants were found to be volatile organic C_2-to-C_8 acids. A comparison between volatile earwax and axillary odors will also be presented. Acknowledgements: NIH postdoctoral training grant (2T32DC000014-32A1) ARO (W911NF-11-1-0087)

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Loss and Recovery of Odorant-Mediated Behavior Correlates with Plasticity of Axonal Projections in the Zebrafish Olfactory Bulb in a Reversible Deafferentation Model

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We have found that the repeated exposure of adult zebrafish olfactory epithelium to the detergent Triton X-100 results in fish losing the ability to respond to odorants associated with social behavior but retaining the ability to respond to odorants linked to feeding behavior. Using a reversible deafferentation technique, we find that fish recover the ability to detect social cues. The aim of the present study was to determine a biological basis for this phenomenon by examining axonal projections after a single treatment with TX-100. Axons of three olfactory sensory neuron subtypes (ciliated, microvillar, and crypt) were identified using immunocytochemistry on paraffin sections. In control bulbs, anti-KLH labeled all glomeruli, while anti-calretinin labeled fewer axons throughout the bulb. Anti-Gas/olf labeling was concentrated in the medial and dorsal bulb, and anti-S-100 labeling was more obvious in the lateral bulb. Within the first 4 days after TX-100 treatment, anti-KLH and anti-calretinin labeling in the deafferented bulb showed an overall reduction, with prominent loss in the medial bulb and preservation of some axons in the lateral bulb. By 7 days, innervation returned to near control levels. Staining in the deafferented bulb with anti-Gas/olf and anti-S-100 was absent 1 day following treatment but returned within 7 days. Examination of the axon patterns showed a selective preservation of certain olfactory sensory axons, while others are temporarily destroyed. The presumptive microvillar axons that survive treatment in the lateral bulb may account for the persistent ability of zebrafish to detect food odorants while the temporary destruction of ciliated axons in the medial bulb is consistent with the loss and recovery of the ability to detect social cues. Acknowledgements: Supported by NIH-NIDCD #011137 (CBJ)

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Coexistence of determined and variable sensory coding strategies in the mouse vomeronasal system

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The mouse vomeronasal organ (VNO) is an important chemosensory subsystem that has been implicated in a variety of social and sexual behaviors. In contrast to combinatorial odor coding by neurons in the main olfactory epithelium, vomeronasal sensory neurons (VSNs) are thought to function as narrowly tuned, dedicated sensors of intrinsically instructive semiochemicals. Here, we investigate the tuning profile(s) of a group of VSNs that are collectively characterized by their sensitivity to a specific class of behaviorally relevant chemosignals: major urinary proteins (MUPs). Using extracellular 'loose-seal' patch-clamp recordings from optically identified basal VSNs in acute coronal VNO slices, we record stimulus-dependent action potential discharge in response to recombinant MUPs, specific for either the C57BL/6J or the BALB/cByJ inbred strain of laboratory mice. Furthermore, we comparatively analyzed the role(s) of these stimuli in two different male-specific behaviors: male-male aggression and territorial countermarking. Surprisingly, electrophysiological activity profiling revealed parallel detection of MUPs by both 'specialist' neurons selectively tuned to a particular stimulus and broad range responders ('generalists') sensitive to all or subset combinations of the MUPs tested. These data suggest the coexistence of determined and variable sensory coding strategies in the mouse vomeronasal system. In addition, behavioral assays indicate that MUPs regulate at least two different male behaviors. While dedicated ligands promote aggression, a combinatorial MUP code controls countermarking. Together, our results show that a vomeronasal stimulus can encode divergent information through both dedicated and combinatorial neural mechanisms.

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Insights into the Function of Darcin from the Three Dimensional Structure

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Mouse urine contains millimolar concentrations of major urinary proteins (MUP) - eight stranded beta barrel lipocalins. MUPs have a broad range of functions in chemical communication between individuals. One MUP, darcin (MGI classification *Mup20*) is highly expressed in males only and is responsible for inherent female attraction to males, the subsequent memory of the volatile odour profile of that male and the rapid induction of memory of the precise physical placement of the scent mark containing darcin. Darcin is responsible for the slow release of the volatile pheromone, 2-*sec*-butyl 4,5 dihydrothiazole. To better understand the unique properties of darcin, we have solved the structure of this protein by NMR. Relative to other MUPs, darcin has a large solvent exposed area and the greatest exposure of hydrophobic residues in the beta barrel. Binding to three ligands – NPN, menadione and a thiazole derivative – were characterized in this study. Menadione and thiazole bound to both darcin and MUP11 in the hydrophobic cavity of the beta barrel, with NMR data indicating a similar binding site for menadione and thiazole in both darcin and MUP11. The largest ligand (NPN) bound only to MUP11, not darcin, suggesting darcin adopts a more compact binding cavity. Darcin is significantly more stable than MUP11, with 92% of darcin structure retained in the native state at 7M urea compared to only 45% in MUP11. The high stability of darcin is consistent with the anomalous migration on SDS-PAGE and a tendency to undercharge in electrospray ionisation mass spectrometers. All this biophysical and ligand binding data point to darcin adopting a more stable and compact conformation with a smaller ligand binding cavity than related MUPs. Acknowledgements: These studies were supported by the Biotechnology and Biological Science Research Council (BB/J002631/1).

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HCN Channels Mediate Proton-dependent Signaling in the Mouse Vomeronasal Organ

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The mouse vomeronasal organ (VNO) plays an important role in the detection of semiochemicals and other social cues. However, many of the basic mechanisms that control VNO physiology remain largely unknown. Here, we investigate proton-mediated activity in the mouse VNO. We show that mouse urine is not only a rich source of social chemosignals, but can also create an acidic environment for such cues. For females, in particular, we find an experience-dependent variation of their generally low urinary pH. Using whole-cell patch-clamp recordings from visually identified sensory neurons in acute tissue slices of the mouse VNO, we show that vomeronasal sensory neurons are activated by protons. We describe that acidic solutions dose-dependently induce inward currents in voltage-clamp measurements and elicit robust action potential firing in current-clamp recordings. Surprisingly, our investigations suggest no substantial involvement of 'classical' candidate proton-activated ion channels. Instead, the pharmacological profile and biophysical properties of the proton-induced responses indicate a critical role of hyperpolarization-activated cyclic-nucleotide-gated (HCN) ion channels in proton-mediated signaling of vomeronasal sensory neurons. Together, our results implicate HCN channel-dependent vomeronasal acid-sensing in gain control of social chemosignaling.

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Kirrel-3 is Required for the Coalescence of Vomeronasal Sensory Neuron Axons into Glomeruli and for Male-Male Aggression

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The accessory olfactory system controls social and sexual interactions in mice that are critical for survival. Vomeronasal sensory neurons (VSNs) form synapses with dendrites of second order neurons in glomeruli of the accessory olfactory bulb (AOB). Axons of VSNs expressing the same vomeronasal receptor (VR) coalesce into multiple glomeruli within spatially

conserved regions of the AOB. Here we examine the role of the Kirrel family of transmembrane proteins in the coalescence of VSN axons within the AOB. We find that Kirrel-2 and Kirrel-3 are differentially expressed in subpopulations of VSNs and that their expression is regulated by activity. While Kirrel-3 expression is not required for early axonal guidance events, such as fasciculation of the vomeronasal tract and segregation of apical and basal VSN axons in the AOB, it is necessary for proper coalescence of axons into glomeruli. Ablation of Kirrel-3 expression results in disorganization of the glomerular layer of the posterior AOB and formation of fewer, larger glomeruli. Furthermore, altered glomerular formation is associated with loss of male-male aggression in *kirrel-3*$^{-/-}$ mice. Taken together our results indicate that differential expression of Kirrels on vomeronasal axons generates a molecular code that dictates their proper coalescence into glomeruli within the AOB. Acknowledgements: Canadian Institutes of Health Research and Natural Sciences and Engineering Research Council of Canada.

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Transduction for pheromones in the main olfactory epithelium is mediated by the Ca^{2+}- activated channel TRPM5

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The main olfactory epithelium contains olfactory sensory neurons (OSNs) that respond to odorants. Interestingly, there is growing evidence that some OSNs in this epithelium respond to pheromones through an unknown transduction mechanism. Here we report on a survey for pheromone transduction in a subset of OSNs expressing the transient receptor potential channel M5 (TRPM5), a Ca^{2+} -activated monovalent cation-selective channel. As in the majority of OSNs, the cyclic nucleotide-gated (CNG) channel subunit A2 is expressed in the cilia of OSNs expressing GFP under control of the TRPM5 promoter. Interestingly these TRPM5-GFP^{+} OSNs lack the Ca^{2+}-activated Cl^{-} channel ANO2 found in the majority of OSNs. Complementary loose patch current and Ca^{2+} fluorescence recordings show that TRPM5-GFP^{+} OSNs respond to pheromones and not to odorants, while TRPM5-GFP^{-} OSNs respond to both. Finally complementary pharmacological and TRPM5 knockout experiments show that TRPM5-GFP OSNs respond to pheromones through the TRPM5 channel. Thus, pheromone responses of TRPM5-GFP^{+} OSNs are mediated by ciliary Ca^{2+} influx through CNG that gates opening of TRPM5. Acknowledgements: Funded by NIH DC006070 and DC004657 (D.R.), CONDECYT 1100682 (F.L.) and CONICYT and MECESUP UCH0713 (J.B.)

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AMYGDALAR PROCESSING OF SALIENT CHEMOSENSORY SIGNALS

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Medial amygdala responds differentially to conspecific and heterospecific chemosensory signals with different meanings and different behavioral responses; and it may be responsible for routing information to hypothalamic/preoptic circuits involved in producing the appropriate responses. The vomeronasal organ (VNO) is the primary but not only source of chemosensory input to medial amygdala but VNO-lesions disrupt the characteristic patterns of responses. The circuit for processing VNO-driven chemosensory input includes the main intercalated nucleus (mICN), one of several GABA-ir ICN cell groups in the amygdala. mICN appears to regulate posterior medial amygdala (MeP) activity similarly to the regulation of central and basolateral amygdala activity by paracapsular ICN cell groups, in the fear conditioning circuit. Using immediate-early gene expression, we previously found that GABA-receptor-ir cells in MeP are suppressed by heterospecific stimuli –as mICN GABA-ir cells are activated. Now using brain slice recording we show hyperpolarization of MeP cells by field stimulation of local mICN. Preliminary evidence also suggests mICN cells are suppressed by bath-applied dopamine, as is the case for paracapsular ICN cells. The amygdala contributes to the motivational/emotional evaluation of sensory inputs of all modalities and for diverse behaviors. This concordance between amygdala processing in completely different types of behavior may indicate some commonalities in circuit organization. Dopamine may be part of a mechanism for modulating amygdala processing of sensory information according to brain state or previous experience. Dopamine appears to modulate experience-dependent chemosensory responses in basolateral amygdala but so far we have not demonstrated an effect in medial amygdala. Acknowledgements: Supported by NIDCD grants R01-DC005813, T32-DC000044 and funding from Florida State University

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Interspecies communication mediated by tear fluids

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Communication between animals are regulated by a variety of chemical cues emitted from the body fluids. Recent works have revealed that exocrine grand-secreting peptide 1 (ESP1), which is released from male mouse tear fluids, enhances female sexual behavior through the vomeronasal organ. This data indicates that the tear fluid is one of the important sources of chemical cues. However, it is unknown whether tear-derived chemical cues mediate only intraspecies communication. In this study, we aimed to understand a novel function of tear fluids in interspecies communication by focusing on tear fluids of rats, a predator of mice. First, we examined the effect of rat tear fluids on the mouse vomeronasal system. c-Fos analysis revealed that rat tear fluids contained some stimulants that induced c-Fos expression in the accessory olfactory bulb (AOB), the first center of the vomeronasal system. It has been known that rats have 10 members of ESP family genes, therefore, we examined whether the stimulants in rat tear fluids are ratESPs. Western blot analysis indicated that ratESP5 and ratESP7 were secreted in rat tear fluids. However, recombinant ratESP5 and ratESP7 did not induce c-Fos expression in the mouse AOB. This data suggests that there exists novel mouse vomeronasal stimulants in rat tear fluids. We next purified the stimulants from rat tear fluids by activity-based fractionation. Amino-terminal peptide sequence and genome analysis revealed that a c-Fos-inducing peptide was encoded by a gene whose function has not been revealed. We named this peptide P18. Recombinent P18 induced c-Fos expression in the AOB of wild type mice, but not in the TRPC2 knock-out mice. These results suggest a possibility that P18 in rat tear fluids mediate interspecies communication through the vomeronasal organ.

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Experience-dependent plasticity causes sexual dimorphism in mouse pheromone-sensing neurons

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In mice, the normal expression of most sex-specific behaviors requires an intact accessary olfactory system (AOS). While the AOS has been long viewed as a sexually dimorphic circuit, the known anatomical differences between males and females consist of modest changes in the packing of neurons in particular brain regions. By themselves, these differences may be insufficient to explain observed dimorphic behaviors. Here we asked whether the first order neurons, AOS sensory neurons differed functionally between two sexes. Using light-sheet based high-speed calcium imaging technique, we recorded ~260,000 individual neurons in intact vomeronasal epithelia from male and female mice. According to the cell responses to 12 sulfated steroids, a class of chemicals that originally isolated from mouse urine, we classified a total of 20, 853 responsive neurons into 17 functional types. We found that the large majority of functional receptor types present in equal abundance in males and females. However, we found clear sexual dimorphism, as two functional types appeared to be male specific, including an epitestosterone-selective receptor type 100-fold more abundant in males than in females. To explore the mechanism generating this dimorphism, we found male specific receptor types became rare after long-term exposure to the odors of female mice, with the result that the vomeronasal organs from males were converted to a pattern indistinguishable from females. This difference in AOS receptor type is by far the strongest sexual dimorphism ever reported in the mammalian central nervous system; that this dimorphism is determined entirely by experience indicates that a sensory system devoted to "innate" responses is strongly modulated by rearing conditions. Acknowledgements: This study was funded by NIH-NINDS/NIAAA Grant R01 NS068409, and NIH Director's Pioneer Award DP1 OD006437(T.E.H.)

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Palatability of Cycloheximide or Caffeine Mixed with Sugar in Hamsters

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Multiple coding mechanisms for bitter stimuli are suggested by taste receptive-field specificity, quality and palatability. Quality and palatability of quinine (Qui), salicin (Sal), caffeine (Caf) and cycloheximide (Cyc) differ in hamsters (*Mesocricetus auratus*). Quality, studied with generalizations of conditioned taste aversions (CTA), differs for each; but, each stimulus is aversive measured in preference to water. Hamster taste aversions are generally reduced by adding sucrose. Thus, aversions to 1mM Qui, 10mM Sal, 30mM Caf and 30μM Cyc were compared to the 4 stimuli mixed with 500mM sucrose. Qui and Sal palatability increased with sucrose added but Caf and Cyc did not (Lloyd et al. 2012). To determine concentration-dependence, 5, 10 and 30mM Caf and 5, 10 and 30mM Cyc (with and without 500mM sucrose) were tested for 2-bottle 48-hr preference vs. water (R-L bottle positions reversed daily). Each hamster randomly received 14 stimuli based on a modified Latin Square. A preference ratio [ml stimulus ingested/ml total fluid ingested; indifference = 0.5] was computed and differences tested with analysis of variance (a =0.05). Hamsters strongly preferred sucrose over water [0.725]. Caf and Cyc aversions were unaffected by concentration or the addition of sucrose. Average preference ratios collapsed across concentration were 0.210 for Caf and 0.225 for Caf + sucrose; 0.164 for Cyc and 0.151 for Cyc + sucrose. Reducing bitter stimulus concentration did not increase amelioration by sucrose. This is consistent with Cyc aversions (1-hr tests) quickly developing, even to Cyc-sucrose mixtures without affecting sucrose intake (Hettinger et al. 2007), and Cyc serving as a CTA UCS when injected IP (Formaker et al. 2009). Acknowledgements: Supported by UConn SDM Alumni Research Fellowship and NIH grant DC004099.

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Regulation of Taste Responses by TNF

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Patients with inflammatory diseases often experience taste alterations. Yet, how inflammation affects taste function is not fully understood. Previously, we showed that tumor necrosis factor (TNF), a potent proinflammatory cytokine, is preferentially expressed in a subset of type II taste cells. The level of TNF in taste cells can be further induced by inflammatory stimuli such as lipopolysaccharide (LPS), a bacterial cell-wall component that elicits acute inflammation. Although TNF plays important roles in mediating inflammation and cell death in various tissues, its roles in taste buds remain to be determined. In this study, we carried out taste behavioral tests and gene expression analyses in wild-type and TNF-deficient mice. Lickometer tests were conducted to examine behavioral responses to salty, sour, bitter, sweet, and umami taste compounds before and after LPS-induced inflammation. Our results showed that TNF-deficient mice were less sensitive to the bitter compound quinine before any treatments. After LPS injection, wild-type mice displayed a range of altered responses to the taste compounds, especially to the sweet taste compound sucrose. In contrast, TNF-deficient mice did not show a significant alteration in response to sucrose after LPS treatment, suggesting that TNF plays an important role in regulating taste response to sucrose under LPS-induced inflammation. Furthermore, gene expression analyses by quantitative RT-PCR showed that the levels of several inflammation- and cell-death-related genes were increased by LPS in wild-type mice, but were not induced in TNF-deficient mice. Together, these results suggest that TNF may be an important mediator for taste dysfunction associated with inflammation. Acknowledgements: This study was supported by NIH/NIDCD grants DC010012 and DC011735.

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Evidence of neonatal memory of odor configuration

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The perception of some mixtures of odorants engages configural abilities, i.e. the perception of these mixtures as single odor objects. For instance, data in human adults demonstrated that a mixture of two odorants (AB), one smelling like strawberry and the other like caramel, generates the configural perception of the odor of pineapple (Le Berre et al., 2008; Barkat et al., 2012). Configural processing may be adaptive also for young organisms, to which rapid extraction of chemical information from the maternal environment, highly complex, is a prerequisite to survival. Thus, results in newborn rabbits suggest the perception of a unique odor in the AB mixture (smelling like configural pineapple in humans) and different from the odors of the elements (Coureaud et al., 2008, 2009a). To clearly demonstrate that the configural AB perception does not directly depend on A and B perception, we investigated here whether rabbit neonates recognize the AB mixture even in the absence of A and B recognition. To that goal, rabbit pups were conditioned to AB on day 1. On day 2, recall of A and recall of B were followed by intraperitoneal injection of either saline or a pharmacological amnesic agent (see Coureaud et al., 2009b, 2011). Testing for behavioral responsiveness to A, B and AB occurred on day 3. Control pups responded behaviorally to AB but also to A and B. As expected, the pups injected with the amnesic agent did not respond to A and to B. However, they responded to AB, indicating an AB perception independent of A and B representations. In summary, the present results confirm the perception by rabbit neonates of a configuration in the AB mixture, and demonstrate for the first time the neonatal ability to memorize odor mixtures as configurations independent of the memory of their elements. Acknowledgements: Supported by French ANR-2010-JCJC-1410-1 MEMOLAP to GC, TTD and GF.

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Sniffing Strategies in Wild-Type and Olfactory Marker Protein Knock-Out Mice

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Detection and identification of an odor requires nasal inhalation or sniffing behavior that delivers odorants to the olfactory receptor neurons (ORNs) deep in the nasal cavity. Our experiments combine behavioral assessment of odor detection and discrimination tasks with measurements of sniffing behavior to clarify the strategies a mouse uses when confronted with odor-based learning tasks and the mechanisms underlying odor perception. We study the behavior and sniffing patterns of mice with (WT) or without (KO) functional olfactory marker protein (OMP), a protein that is responsible for speeding up the time course of odor-induced responses in ORNs. OMP KO and WT mice were implanted with wireless pleural pressure sensors to record sniffing patterns. These mice were then trained and tested in go/no go odor discrimination tasks to distinguish solvent (mineral oil) odor from the odor of 1-propanol 10^{-4} log dilution. Upon propanol or solvent exposure, WT mice increased their sniffing rate from ~4 Hz to 10 Hz and maintained a higher sniffing rate for rewarded (S+) trials. However, KO mice continued to increase their sniff rate following the onset of the odor (S+) and solvent-odor cues (S-) significantly in comparison to the WT mice (p <0.05). This suggests that OMP KO mice require more stimulation cycles to determine the identity of an odor cue in contrast to OMP WT mice, which make a determination quickly and begin to decrease sniff frequency immediately following odor onset. Understanding the temporal relationship of both sniffing frequency and the duration of odor sampling in OMP WT and KO mice, in combination with biophysical data on odor responses obtained from individual ORNs isolated from these mice, will help elucidate the role of OMP in olfactory transduction and odor-investigation strategies. Acknowledgements: This research is supported by R01 DC009613 and based upon work supported by the U. S. Army Research Office under grant number W911NF-11-1-0087. Sensor implantation was performed at The Behavioral and Physiological Phenotyping Core, which is supported, in part, by funding from the NIH-NIDCD Core Grant 1P30DC011735-02.

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The Temporal Structure of Odor Mixture Perception in Rats

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Temporal structure of odor mixtures is often overlooked, but this is what gives many mixtures their complex percepts. This structure can help us understand the puzzling qualities of odor mixtures. There is not yet any theory that can predict whether a mixture of 2 monomolecular odorants will smell like both odors (elemental), like one more than the other (overshadowing), or like neither (configural or synthetic). One feature that is often overlooked in studies of mixture perception is the difference in perceptual arrival time for the two odors. These delays have been measured in humans, but implementing these sensitive perceptual assays in rats is much more difficult. We have developed a task that allows us to do this in rats, using a combined 2-alternative choice - go/no-go paradigm. The results show that behavioral response profiles to timing differences in binary mixtures are specific to the odor pair and that the responses to positive and negative delays are not symmetrical. For example, at zero delay (only the natural processes producing delays) in a 1:1 mixture of amyl acetate and anisole, anisole overshadows amyl acetate. As anisole is moved earlier in time overshadowing becomes stronger. In the negative direction, with amyl acetate preceding anisole, the mixture enters a configural regime at -50ms to -200ms and then takes on an elemental quality at -250ms. These results suggest that in the temporal domain, elemental and configural responses are close, with overshadowing responses occupying a separate part of the temporal space. The properties of odorants, such as sorptiveness and volatility, that may contribute to temporal effects are discussed. Acknowledgements: Institute for Mind and Biology Seed Grant (LK) Hodson Research Fellowship (CD)

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The Fine Temporal Structure of the Rat Licking Pattern: What Causes the Variability in the Interlick Intervals and How is it Affected by the Drinking Solution?

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Licking is a repetitive behavior controlled by a central pattern generator. Even though interlick intervals (ILI) within bursts of licks are considered fairly regular, the conditions that affect their variability are unknown. We analyzed the licking pattern in rats that were licking water, 10% sucrose solution, or 10% ethanol solution, in 90 min recording sessions after 4 h of water deprivation. The histograms of ILIs indicate that licking typically occurred at a preferred ILI of about ~135 ms with evidence of bi- or multi-modal distributions due to occasional licking failures. The longer the pause between bursts of licks (≥3 consecutive licks with ILIs <200 ms), the shorter was the first ILI of the burst. When bursts of licks were preceded by a pause >4 sec, the ILI was the shortest (~110 ms) at the beginning of the burst and then it increased rapidly in the first few licks and slowly in subsequent licks. The first ILI of a burst of licks was not significantly different when licking any of the 3 solutions, but subsequent licks exhibited a temporal pattern characteristic of each solution. Moreover, rats licked the ethanol solution in shorter bursts and the sucrose solution in longer bursts when compared to water. Therefore, rats may rapidly identify the fluid and modify their licking behavior by adjusting the temporal pattern of licks and the number of licks/burst. The rapid deceleration in licking rate in bursts of licks that occurred after >4 sec pause was due to an increase from ~27 ms to ~56 ms in the tongue-spout contact duration while the intercontact interval was only slightly changed (80-90 ms). Therefore, the contact duration seems to be the major factor that increases the variability in the ILIs, and could be another means for the rat to adjust the amount of fluid ingested. Acknowledgements: Grant P20 GM103425-09

#P205

POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

How do rabbit newborns and human adults perceive the configuration in a 6-component blending odor mixture?

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Comparative studies give the opportunity to better understand common and dissimilar processes in terms of perception, cognition and behavior between organisms. Regarding the elemental and configural perception of odor mixtures, newborn rabbits and human adults present some similarities. In particular, they both process a 6-component mixture (RC) in a weak configural way, leading to the perception of a novel odor (e.g., red cordial in humans) in the mixture: in rabbits, neonates do not respond to RC after learning of one component, while they generalize for another mixture of same complexity; in humans, the quality of the single odorants is judged as significantly different to the mixture. Here, we set out to examine whether the perception of the RC configuration strictly depends on the quantity and/or the quality of the components. To that goal, we carried out a generalization experiment in rabbit pups and a similarity rating task in human adults, using several sub-mixtures of increasing complexity (i.e., 2, 3, 4 or 5 odorants). We conditioned the pups to sub-mixtures and tested their behavioral responsiveness to these stimuli compared to the full mixture (RC). In humans, participants rated the similarity between the sub-mixtures and RC. The results indicated that newborn rabbits became able to respond to the RC mixture when they had previously acquired at least 4 of its components, whatever their odor quality. In human adults, similarity between sub-mixtures and the RC mixture depended more on the odor quality of the odorants included in sub-mixtures rather than on the number of mixed odorants. Therefore, even if these two models shared a configural perception of the same RC odor mixture, the factors underpinning its perception seem to be different, at least in part.

#P206

POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

The Contribution of the T1R1 Subunit to Taste Detection of Glutamate as Behaviorally Assessed in a Murine Model.

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Whether taste detection of L-glutamate is mediated solely by the T1R1+T1R3 heterodimer or whether an additional glutamate-sensing taste transduction mechanism(s) contributes is controversial. Here, we behaviorally assessed the necessity of the T1R1 subunit to taste detection of monosodium glutamate (MSG) in a two-response discrimination procedure using T1R1 knockout (KO) mice and their same-sex littermate wild-type (WT) controls. Water-restricted mice were trained to discriminate a tastant from water with a correct response resulting in the delivery of a water reinforcer and an incorrect response resulting in a time-out. Sensitivity to NaCl and MSG was similar between genotypes. However, upon the addition of the sodium channel blocker amiloride (100 μM) and inosine 5' monophosphate (IMP), at a concentration (2.5 μM) shown to potentiate the glutamate signal in a variety of assays, performance of the KO mice to this MSG mixture (M+A+I) was severely impaired. Whereas WT mice performed at consistently high levels across concentrations, the ability of the KO mice to detect the M+A+I solution was above chance only at the higher MSG concentrations. The possibility that IMP was precluding concentration-dependent performance in the WT mice to the MSG in the presence of amiloride was confirmed when we found that WT mice could detect 2.5 μM IMP alone with relatively high accuracy, whereas KO mice could not respond significantly above chance. Collectively, these results strongly suggest that 1) the Na^+ ion dominates the taste detection of MSG in mice consistent with other recent data from our laboratory, and 2) glutamate may be activating a T1R1-independent high-threshold receptor in the presence of IMP, but normal detection of glutamate depends on the T1R1 subunit. Acknowledgements: NIH R01-DC004574 (ACS) & NSF GRF to KRS

#P207 POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

A Role for Salivary Proteins in Taste Mediated Behavior

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While few studies have examined the influence of salivary proteins on taste-mediated behavior, it has been demonstrated that salivary proline-rich proteins (PRPs) bind to bitter-tasting tannic acid (TA) and may function to increase the acceptability of TA-containing diets. To test this hypothesis, we collected saliva samples and measured spontaneous feeding behavior in rats (n=8) fed a control diet (16 days) followed by a diet containing 3% TA (12 days). Total intake was reduced during the first 3 days of the TA diet ($p<0.01$). This reduction was due to a decrease in meal size (g/meal, $p<0.01$), a measure of postingestive feedback. Total intake and meal size recovered to base line levels during the TA treatment. These increases in meal size and total intake were significantly correlated with increases in the expression of PRPs ($p's \leq 0.02$), which were present in saliva by the third day. TA treatment also decreased rate of feeding (g consumed/sec, $p<0.01$), a measure of palatability. Although there was an increase in rate of feeding during the treatment, which was significantly correlated with PRP production ($p=0.03$), this measure did not return to base line levels. To examine palatability in the absence of postingestive feedback, rats were given TA at varying concentrations (0-3%) in a brief-access test while PRPs were either increased (by tannin exposure, n=6) or unchanged (maintained on a control diet, n=6) in a second experiment. Rats with PRPs present in the saliva licked more, in 10s, to intermediate concentrations of TA (0.09 and 0.18%, $p's<0.04$) than rats without PRPs. Together, these data suggest that PRPs play a role in altering both the palatability and postingestive feedback associated with TA. Acknowledgements: NIH-DC-000044, DK-73936, DC-004785, DC-012632

#P208 POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Adaptive respiratory behavior communicates social hierarchy in rats

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Sniffing behavior is regularly displayed by terrestrial vertebrates during social interactions. No measures of sniffing from interacting animals are available, however, calling into question the utility of this behavior within the social context. Here I found that investigation by a dominant rat towards the facial region of a subordinate often elicits a concomitant decrease in respiratory frequency in the subordinate animal. Failure of subordinates to decrease their respiratory frequency in this context shortened the latency for agonistic behavior by dominant rats, reflecting that decreases in respiratory frequency serve as appeasement signals. Rats rendered unable to smell displayed reciprocal respiratory behavior, demonstrating the independence of this behavior for gathering odors or sharing odor stimulus space. Oxytocin treatment abolished agonistic behaviors and reciprocal respiratory displays. These findings demonstrate a novel form of communication in rodents, by showing that rodents utilize sniffing behaviors communicatively, not only to collect, but also to convey information. Acknowledgements: NSF grant IOS-1121471

#P209 POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Discrimination of homologous alcohol odorants varying in carbon chain by behaviorally-trained Fisher F344 rats

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Recent studies suggest that chemicals varying in carbon chain length may represent a generalization gradient among odorants. To investigate how odor quality is reflected perceptually in the rat, we measured graded perceptual similarity by varying carbon chain length across a series of homologous alcohol pairs. We employed an automated, liquid-dilution olfactometer to train

F344 rats on a two-odor discrimination task. Six odorants (1-propanol, 1-butanol, 1-pentanol, 1-hexanol, 1-heptanol and 1-octanol) were arranged to produce 30 novel odorant pairs differing between one and five carbon atoms; testing sessions included presentation of only one randomly assigned pair daily (200 trials daily). Results showed that, although rats learned to discriminate between any two odorant pairs, discrimination accuracy changed systematically with carbon chain length difference. Error patterns were remarkably consistent across animals, such that marked increases in misses and false alarms were indicated for pairs differing by one or two carbon atoms. Across all odorant pairs, these effects were most pronounced during the first 20 trials. Notably, the greatest degree of perceptual confusion was displayed for two pairs differing by a single carbon atom, 1-propanol/1-butanol and 1-heptanol/1-hexanol. These data provide further support for carbon chain length as an important odorant stimulus dimension for study of olfactory receptor interaction (Johnson and Leon, 2000) as well as demonstrate how hierarchical chemotopic organization of the olfactory bulb may be reflected perceptually. Furthermore, development of an animal model using the carbon chain paradigm may be useful for assessing the mechanisms underlying olfactory dysfunction.

#P210 **POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION**

The Gustatory Stop-Signal Task: A Method for Measuring Taste Quality Discrimination in Mice with Millisecond Temporal Resolution

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There is a lack of consensus regarding the roles of temporal and spatial coding of taste quality in the gustatory system due in part to various experimental and analytical differences among previous studies. Quantitative behavioral analysis can be used to test for the cognitive principle of speed-accuracy tradeoff (SAT), a hallmark of temporal processing of sensory stimuli. However, current methods used to study taste perception in rodents are temporally too slow for precise reaction-time measurements required to test for SAT in the gustatory system. We designed a novel behavioral paradigm, the Gustatory Stop-Signal Task, in head-restrained mice for measuring perceptual identification of taste stimuli with millisecond temporal resolution. Using this new paradigm, we will apply threshold psychophysics to determine if a stimulus-dependent SAT is present during discrimination of basic tastes. This will provide crucial behavioral evidence for the potential roles of temporal and spatial coding strategies underlying taste quality coding in the gustatory system. Additionally, the task can be combined with advanced physiological techniques, such as visually guided whole-cell patch-clamp recordings in sub-regions of gustatory cortex. The gustatory stop-signal task in head-restrained mice will provide a new foundation to combine precise quantitative behavioral measurements of taste perception alongside state-of-the-art in vivo physiology. Acknowledgements: NIH Grants R01 DC00407 and F32 DC012461 - 01A1

#P211 **POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION**

Free Access to Highly Palatable Food during Adolescence Increases Anxiety- and Depression-like Behaviors in Males, but not in Females

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We have reported that a long-term access to highly palatable food (HPF) modulates the hypothalamic-pituitary-adrenal (HPA) axis response to restraint stress in adult male rats. Psycho-emotional disorders frequently involve dysfunctions in the HPA axis activity. In this study, male and female SD rats had free choices of chocolate cookies as HPF and chow with *ad libitum* access from PND 28, and then were subjected to behavioral tests at youth. Control group received chow only, and food conditions were continued throughout the whole experimental period. Body weight gain and daily caloric intake did not differ between HPF and control groups both in males and females. Total ambulatory activity was decreased with HPF access in females, but not in males. However, HPF increased anxiety related behaviors in males; i.e. increased rostral grooming and decreased the open arms stay during elevated plus maze test, but did not affect those indexes in females. Immobility duration during forced swim test was significantly increased with HPF access in males, but the increase was not reached to a statistical significance in females. Stress-induced corticosterone increase was shortened with HPF access both in males and females. Results suggest that adolescence free access to highly palatable food may lead to a dysfunction in the HPA axis activity both in males and females; however, its psycho-emotional outcome be worse in males. Acknowledgements: Supported by MOEST(2009K001269 2010-0003642)

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POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Licking Microstructure Reveals Rapid Attenuation of Neophobia

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Neophobia—the initial hesitation that many animals show to a novel food—is typically measured by comparing consumption in the first and second sessions of access to the taste; lower consumption in session 1 denotes neophobia, and higher 2nd-session consumption denotes attenuation of neophobia (AN). AN is thought to represent a *bona fide* example of learning—neural plasticity induced by an association between the taste and a safe outcome on session 1 changes the response to the tastant during session 2. Such long-term plasticity processes require time to complete, and thus AN should only stabilize 90 min or more following the first exposure to the tastant—a prediction that has been borne out in behavioral data. It remains possible, however, that a more rapidly developing AN might escape detection in time-averaged accounts of behavior such as consumption. With this in mind, we performed a comparison of AN in two contexts, a two-bottle test and a brief access test (which allowed a real-time analysis of licking microstructure). At the level of overall consumption, data from the two tasks were in good accord—both revealed AN to 28mM saccharin but not to 2.8mM saccharin. Additionally, however, the brief access task revealed an initial hesitation to consume the higher concentration saccharin solution; this seemingly neophobia-related hesitation not only decreased between sessions 1 and 2, but also decreased linearly across the twenty minutes of session ; that is, AN began within minutes of the rats' first exposure to the taste. These data validate the brief-access task as an paradigm with which to measure AN, and also reveal aspects of AN—perhaps related to short-term plasticity—that appear within minutes of the first taste. Acknowledgements: National Institutes of Health, World of Work Fellowship

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POSTER SESSION IV: CHEMICAL SIGNALING AND BEHAVIOR; ANIMAL BEHAVIOR/PSYCHOPHYSICS; CHEMOSENSATION AND METABOLISM; VOMERONSASAL AND CHEMICAL COMMUNICATION

Channelrhodopsin Mice use Temporal Information Encoded in the Olfactory Bulb for Odor Sensation.

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Odor information is represented by spatio-temporal maps in the olfactory bulb (OB). Spatial maps reflect the converging axons of olfactory receptor neurons activated by odors, onto their respective glomeruli in the OB. The origins of temporal patterns of glomerular activation are less well understood, but odorant receptor affinity as well as odorant sorption kinetics across the olfactory epithelium could underlie temporal parameters such as onset latency and rise time. Consistent differences in response dynamics across glomeruli have been found for odor-evoked responses in the OB. Further, we have shown, using optical imaging that retronasal and orthonasal bulbar reponses differ in response amplitude as well as temporal dynamics. It is therefore evident that rich temporal information is available in the bulbar response. However it is not known whether these temporally dynamic responses are behaviorally relevant. Using transgenic mice expressing ChR2 under the Thy-1 promoter in the mitral cells and a digital micromirror device to project sniff-triggered light patterns onto the dorsal OB we are able to exert tight spatio-temporal control over OB activity patterns. We find that mice trained on a go/no-go task are able to discriminate patterns that are spatially identical but differ temporally. By varying the relative delay among the same regions activated by light patterns we are able to determine the threshold of temporal discrimination. We find that Thy-1 ChR2 but not wild-type mice can make temporal discriminations of less than 30ms. Our optogenetic study confirms that awake, behaving mice can use temporal information encoded in the bulbar response. This suggests that temporal coding can contribute to retronasal and orthonasal odor sensation. Acknowledgements: This work is supported by NIH/NIDCD Grants R01DC009994 and R01DC011286 and NIH Institutional Training Grant T15-LM007056 from the National Library of Medicine.

#P214 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Potentiation of Primary Afferent Innervation in the Rostral Nucleus of the Solitary Tract

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The development of mature primary afferent circuitry results from a Hebbian-like synaptic strengthening in a number of sensory systems. This synaptic strengthening is accompanied by a pruning of non-strengthened inputs resulting in a mature terminal field anatomy. Gustatory afferents innervating the oral cavity project to the rostral nucleus of the solitary tract (rNTS), the terminal fields of which prune between postnatal days 15 and 60 into an adult-like organization. However, it is not known whether any activity dependent changes in synaptic strength can be induced during this period that may correspond to the anatomical remodeling. To investigate the activity-modulated plasticity of primary afferent inputs to the rNTS, acute horizontal rNTS slices were prepared from rats of postnatal ages covering the period of anatomical plasticity. The solitary tract was stimulated with a concentric bipolar electrode and excitatory postsynaptic currents (ePSC) were recorded. The ability of a synapse to be potentiated was investigated by stimulating the solitary tract at 50 Hz paired with a 5 ms depolarization. Following this tetanic stimulation increases in ePSC amplitude and rise slope were observed in each age examined, though only in a subset of neurons at each age. Interestingly, the probability of inducing potentiation appears to decrease between postnatal days 20-25 and subsequently increases from postnatal day 30 onward. Primary afferent potentiation lasted over variable time scales ranging from 1 to 30 minutes, indicative of either short-term or long-term potentiation. These results suggest that subpopulations of primary afferent synapses can be potentiated throughout development, and the presynaptic nerve and/ or postsynaptic target specificity for this potentiation will the focus of future studies. Acknowledgements: T32DC000011, RO1DC000288

#P215 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Ephrin-B/EphB signaling influences the innervation of fungiform papillae

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Geniculate ganglion axons innervate fungiform taste buds whereas the trigeminal ganglion neurites innervate the adjacent non-taste epithelium. Owing to the proximity of their terminal fields, non-diffusible repellents are likely to have a role in preventing incorrect targeting. Eph receptors and ephrins are cell-attached receptor/ligands capable of triggering contact-dependent repulsion or stabilization. An antibody that detects EphB1, B2, and B3 stains both geniculate and trigeminal axons throughout embryonic development. Anti-ephrin-B1 and anti-ephrin-B2 labeled the dorsal lingual epithelium uniformly at E17, when axons first penetrate the papilla epithelium in rat. In ephrin-B2 lacZ mice, label was also observed throughout the dorsal epithelium but only from E16.5, well after initial invasion of axons into the epithelium (E14.5). However, in ephrin-B1 lacZ mice, only fungiform papilla epithelium was labeled, and this labeling was observed at E14.5. Mice lacking EphB1 and EphB2 exhibited normal levels of gustatory innervation at E13.5, but less innervation than controls by E17.5, suggesting that ephrin-B/EphB forward signaling may have a stabilizing influence on gustatory afferents in vivo. In vitro, substratum stripes prepared from high concentrations of ephrin-B2-Fc (40 ug/ml) repel neurites from both the geniculate and trigeminal ganglia, and this did not depend on which neurotrophin was used to promote growth. Stripes prepared from lower concentrations of ephrin-B2-Fc (4 ug/ml) were not repellent; indeed, coverglasses coated uniformly with 4 ug/ml ephrin-B2 mildly promoted trigeminal neurite outgrowth length, depending on the stage and neurotrophin. We are currently analyzing the effects of ephrin-B1 on geniculate and trigeminal neurites. Acknowledgements: 1R15DC010910-01

#P216 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Glial Contributions to the Formation of the Solitary Tract and the Rostral Nucleus of the Solitary Tract

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The solitary tract (ST) consists of afferent fibers that originate in the oral cavity and project to the rostral nucleus of the solitary tract (rNST), the site of the first synaptic relay in transmitting taste-related information to higher brain areas. We are interested in the regulatory elements that direct ST formation and rNST development. Glia represent approximately half of the cells in the CNS and play roles in neuron guidance and synapse development and function. However, the time course of glial development and the role of glia in the gustatory brainstem are unknown. We surveyed the expression of glial and neuronal markers in the pre- and post-natal developing rat ST and rNST to characterize their contribution to the development of the gustatory brainstem. We examined the expression of neuronal markers, including calbindin and NeuN, and glial markers, including glial fibrillary acidic protein (GFAP), myelin basic protein (MBP) and brain lipid binding protein (BLBP), in conjunction with P2X2, a marker of gustatory nerve terminal fields, in the developing ST and rNST. We found persistent but dynamic expression of calbindin, GFAP and BLBP throughout pre- and post-natal development. In particular, GFAP expression shifts from more fibrillary to more astrocyte-like labeling in the

early postnatal period. This shift is concurrent with terminal field plasticity, i.e., developmental remodeling and fine-tuning of circuits. Furthermore, the GFAP-positive astrocyte-like cells are differentially distributed throughout the rNST. This work highlights potential neuron-glia interactions that are important for the development of the gustatory brainstem. The results provide basic information for building mechanistic studies regarding glial function in taste circuit formation. Acknowledgements: NIH NIDCD Grant DC009982

#P217 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Functions of the GDNF family of neurotrophic factors in the development of the peripheral gustatory system

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During development of the peripheral nervous system (PNS), target-derived neurotrophic factors, such as the neurotrophins and the glial cell-line derived neurotrophic factor (GDNF) family ligands (GFLs), are critical for the establishment of proper connections between neurons and their targets. The four GFLs, GDNF, neurturin (NRTN), artemin (ARTN) and persephin (PSPN), are potent growth, guidance and survival factors for both PNS and CNS neurons. The GFLs bind with high affinity to GPI-anchored coreceptors called the GFRalphas, of which there are four (GFRalpha1-4). In the PNS, these GFL-GFRalpha complexes then associate with and activate their common receptor tyrosine kinase, Ret. Several of the GFLs and their receptors are expressed by components of the peripheral gustatory system. GDNF and NRTN are expressed throughout the lingual epithelium, and GDNF, GFRalpha1, GFRalpha2 and Ret are all expressed in taste buds of circumvallate papillae. In addition, neurons of the petrosal and geniculate ganglia express Ret and cognate GFRalphas. It is not known, however, whether GFLs function in the development and maintenance of peripheral gustatory circuits. Using conditional transgenic deletion of Ret, we are in the process of determining whether the GFL/Ret signaling pathway is necessary for the development of fungiform papillae, taste buds within circumvallate and fungiform papillae, and their respective innervation by petrosal and geniculate neurons. These studies will establish whether other neurotrophic factors besides BDNF and NT-4 have developmental functions in the embryonic morphogenic events in the lingual epithelium necessary for papillae and taste bud development, as well as growth and survival functions for the sensory neurons that innervate these lingual structures. Acknowledgements: BAP: NINDS R01 NS058510 CRD: NIDCR TEAM Tissue Engineering and Regeneration Training Grant T32 DE007057

#P218 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

The p75 receptor regulates gustatory innervation patterns during development

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As a pan receptor of neurotrophins, p75 can function as either a pro-survival or pro-death factor during development. P75 is expressed in both taste buds and taste (geniculate) neurons; however, the role of p75 receptor during taste development is unclear. Here we examined the role of p75 in neuron survival, taste bud formation and peripheral innervation patterns during development. We found that $p75^{-/-}$ mice began to lose about 22% ($p=0.05$) of geniculate neurons compared to the wild type mice at E14.5, and the loss continued to around 36% ($p<0.05$) by E18.5. At birth, taste bud number was reduced in $p75^{-/-}$ mice (60 ± 4, $p<0.05$) compared to wild type mice (103 ± 7). Remaining taste buds consisted of two-populations, larger innervated taste buds and smaller un-innervated ones. The loss of innervation to taste buds was much greater than would be expected from the neuron loss, indicating that innervation could also be disrupted. Using DiI-labeling and immunohistochemistry, we found that taste nerve growth was delayed and normal innervation patterns were disrupted in $p75^{-/-}$ mice. Interestingly, the pattern of disrupted innervation in $p75^{-/-}$ mice was unique and did not resemble that of other neurotrophin knockouts. At E14.5, which is the first day of target innervation, few axons reached the tongue epithelium in $p75^{-/-}$ mice. At E16.5, innervation patterns in $p75^{-/-}$ mice were still disrupted, some fiber bundles were seen innervating the tip and back of the tongue; however, innervation to the fungiform papillae in the middle area of the tongue was lost in $p75^{-/-}$ mice. This loss of innervation was not rescued at a later age, E18.5. Taken together, these results indicate that while p75 may mediate neurotrophin support of taste neuron survival, it has a unique role in establishing peripheral innervations patterns. Acknowledgements: National Institutes of Health Grant DC009418.

#P219 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

***Lgr5* Expression Defines a Set of Progenitors that Give Rise to Both Taste Cells and Keratinocytes of Adult Mouse Circumvallate and Foliate Papillae**

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Lingual taste cells continually turn over in adult mammals; however, the source and properties of regenerative cells remain unknown. Wnt signaling plays critical roles in several renewing tissues, and the Wnt target *Lgr5* has been identified as a *bona*

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fide adult stem cell marker. Because canonical Wnt signaling is activated at sites of mature taste buds, we asked if *Lgr5* expression identifies analogous stem/progenitor cells in the taste system. Knock-in mice with the *Lgr5-EGFP-ires-CreERT2* transgene replacing one *Lgr5* allele were bred to the tamoxifen (TM)-inducible mTmG reporter strain. The progeny express soluble GFP (sGFP) under endogenous *Lgr5* regulation and, following TM treatment, membrane-bound tdTomato (mT) is replaced by GFP (mG). sGFP is present in all papillae of 7 day-old non-induced mice, but by 12 weeks of age is seen only in circumvallate (CV) and foliate papillae. Expression in the CV is highest where salivary ducts intersect papilla walls, decreases dorsally in the papilla, and is absent from taste buds. In salivary ducts, sGFP is limited to the outer layer of the bi-layered epithelium. One day after a single TM injection, induced mG marks small round cells at the papilla base and, rarely, in the lateral wall of the CV papilla. By 2-3 days post-injection, labeled cells lie both within taste buds and in the surrounding stratified epithelium. Although mG-positive cell numbers decline by 7 days, induced labeling is still apparent in taste buds after 2 months. Importantly, we found no evidence for TM-induced labeling of cells outside of taste papilla boundaries. These data indicate that *Lgr5* expression marks long-term taste cell progenitors, that Lgr5 may be a regulator of taste epithelium homeostasis, and that a duct-basal trench-papilla axis of epithelial renewal may exist. Acknowledgements: Supported by NSF REU #1062645

#P220 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Temporal and spatial differences in BDNF and NT4 expression determine their unique roles in gustatory development

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A limited number of growth factors are capable of regulating numerous developmental processes, but how they accomplish this is unclear. In the gustatory system, brain-derived neurotrophic factor (BDNF) and neurotrophin-4 (NT4) have different developmental roles but exert their effects through the same receptors (TrkB and p75). Using genome wide expression analysis, we determined that BDNF and NT4 regulate the expression of different sets of genes downstream of receptor signaling in gustatory ganglion. These differences in gene expression likely determine their different roles during development. BDNF and NT4 could function differently because of temporal or spatial differences of expression or the activation of different signaling pathways. Using mice in which the coding region for BDNF is replaced with NT4 ($Bdnf^{Nt4/Nt4}$), we show that NT4 can mediate most of the unique roles of BDNF. Specifically, caspase-3-mediated cell death, which is increased in $Bdnf^{-/-}$ mice ($p<0.01$), was rescued in $Bdnf^{Nt4/Nt4}$ mice, and the number of caspase-3-meidated cell death was even lower than that in wild-type mice ($p<0.05$). In BDNF knockout mice, taste bud innervation in the tongue was disrupted, and gustatory axons failed to reach their targets. However, the disrupted innervation was recovered and targeting is normal when NT4 replaced BDNF. The expression of differentiation-, apoptosis- and axon guidance-related genes was down-regulated in the geniculate ganglion of BDNF mutant mice ($p<0.05$), but replacement by NT4 rescued all gene expression changes. These findings indicate that the functions of BDNF and NT4 in taste development are interchangeable. Spatial and temporal differences in neurotrophin expression can regulate differential gene expression *in vivo* and determine their specific roles during development. Acknowledgements: DC009418 and DC007176

#P221 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Detailed expression analysis of a neural crest-specific *P0-Cre* transgenic mouse line and comparison with *Wnt1-Cre*

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We have recently reported that both *Wnt1-Cre* and *P0-Cre* labeled neural crest derived cells are located in tongue epithelium, taste papillae and taste buds, suggesting a neural crest contribution to taste bud cells. However, the difference is profound between *Wnt1-Cre* and *P0-Cre* lines in proportions and distribution patterns of neural crest derived cells in tongue epithelium, i.e., abundant *P0-Cre* labeled epithelial cells versus few cells in *Wnt1-Cre* mouse. Such differences in distributions between *Wnt1-Cre* and *P0-Cre* labeled cells are also found in other systems. To better interpret the data using *Wnt1-Cre* and *P0-Cre* mouse lines for neural crest derivation assays, we made a detailed expression analysis of the *P0-Cre* transgenic mouse line at early embryonic stages in comparison with *Wnt1-Cre* using an *R26R* reporter. We found that *P0-Cre* driven reporter expression emerges in the cranial neural crest region at E8.5 (6-somite stage) and is more profound in hindbrain than midbrain. This is in contrast to the distribution pattern of *Wnt1-Cre* labeled neural crest cells, which is extensive in midbrain but with far fewer cells in hindbrain. The *P0-Cre* labeled cells are largely co-localized with neural crest stem cell markers p75, Slug, AP2 and Sox 9. Combined with our findings that *P0-Cre* labeled cells are far more abundant than *Wnt1-Cre* in lingual epithelium, including taste papillae and taste buds, the data suggest that *Wnt1* and *P0* mark overlapping but different subpopulations of neural crest cells, and that the hindbrain is the primary region of neural crest cells that contribute to taste papillae and taste buds. Acknowledgements: NIDCD NIH Grant R03DC009055 and R01DC012308 to HXL, NIDCD R01DC000456 to CMM, NIDCR Grant R01DE020843 to YM

#P222 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

Multiple Shh Signaling Centers in Embryo and Adult Participate in Fungiform Papilla and Taste Bud Formation and Maintenance

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Fungiform papillae must contain long-lived sustaining cells and short-lived maintaining cells that support development, differentiation and maintenance of the lateral and apical papilla epithelium and the specialized taste buds. *Shh* is a known regulator of papilla development but details about locations of ligand, target responding cells and transcriptional activators for *Shh* signaling are not known. We used immunostaining, in situ hybridization and reporters for *Shh*, *Ptch1*, *Gli1* and *Gli2*-expressing cells to identify proliferating and differentiating cells in embryonic, postnatal and adult tongue, in papilla placodes, fungiform papillae and/or taste bud cells that participate in *Shh* signaling. Whereas there is a progressive restriction in location of the Shh ligand, a receptive surround of *Ptch1* and *Gli1* expression in responding cells is maintained in particular epithelial and mesenchymal signaling centers throughout papilla development and taste bud differentiation. From lineage tracing, we know that *Gli1*-expressing cells and their progeny are located in fungiform papilla basal cells, in perigemmal cells and mesenchymal cells of the papilla core, and are progenitors of taste cells. Further, using a doxycycline-regulated bitransgenic *GLI2** mouse, in a functional test of activated *Shh* signaling in postnatal tongue epithelium, there is loss of filiform papilla spines and loss of fungiform papillae and taste buds. Loss of papilla organs is accompanied by proliferation in suprabasal layers of the lingual epithelium. The synthesized data position *Shh* signaling in multiple centers that are essential to placode and papilla development, and to postnatal papilla and taste bud differentiation and maintenance. *Shh* roles are most likely via paracrine mechanisms, and engage epithelial/mesenchymal interactions. Acknowledgements: NIH Grants NIDCD DC000456 (CMM), NIDDK DK065850 (DLG), NCI CA087837 (AAD).

#P223 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

BDNF is Required for the Development of Adult Taste Bud Number and Normal Behavioral Responses to Sour Stimuli

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Brain derived neurotrophic factor (BDNF) regulates gustatory system development. Because BDNF removal is neonatal lethal, the long-term effects of BDNF removal on the structure and function of the adult gustatory system are unclear. To address this issue we examined the adult taste system in conditional *Bdnf* knockouts in which *Bdnf* expression is reduced to one-tenth normal levels in the entire animal (*Bdnf* $^{lox/lox}$) and is completely removed from the lingual epithelium (K14-Cre;*Bdnf* $^{lox/lox}$). K14-Cre;*Bdnf* $^{lox/lox}$ mice had very few fungiform taste buds remaining (11 ± 2) compared to wild type (52 ± 5, $p \leq 0.002$) or *Bdnf* $^{lox/lox}$ mice (42 ± 10; $p \leq 0.02$). The K14-Cre;*Bdnf* $^{lox/lox}$ circumvallate papillae contained 25% fewer taste buds than the control genotypes ($p \leq 0.025$). There was no difference in taste bud number between wild type and *Bdnf* $^{lox/lox}$, even though *Bdnf* $^{lox/lox}$ mice have substantially reduced *Bdnf* expression. Therefore, as long as some BDNF remains, normal taste bud numbers are maintained. Short-term lick rate tests of K14-Cre;*Bdnf* $^{lox/lox}$, *Bdnf* $^{lox/lox}$, and wild type mice were used to examine taste function. Surprisingly, in spite of the large reduction in taste bud number, there was no statistical difference among the genotypes in lick rates to sucrose, quinine, and NaCl. This indicates that normal behavioral taste responses can be maintained in mice with few fungiform taste buds. However, K14-Cre;*Bdnf* $^{lox/lox}$ mice have higher lick rates to citric acid at pH=3.2 ($p \leq 0.024$) and pH=2.8 ($p \leq 0.01$) compared to wild type mice. This indicates that removal of BDNF may cause a specific deficit in sour taste, which cannot be explained simply by the loss of taste buds. Acknowledgements: DC007176

#P224 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

Reorganization of Primary Afferent Terminal Fields in the Mouse Brainstem Produced by Early Prenatal Dietary Sodium Restriction

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Age-related decreases in terminal field volumes of the rat GSP, CT, and IX nerves and their overlapping fields in the nucleus of the solitary tract (NST) occur during normal development. The processes involved in "pruning" the three terminal fields can be altered significantly when rats are fed a sodium-restricted diet from E3-E12. All terminal fields are relatively large during early postnatal ages and thereafter fail to "prune". Surprisingly, many of the terminal fields in restricted rats expand after 35 days

postnatal. Thus, a very early period of dietary sodium restriction leads to a late-onset expansion of terminal fields in the rat NST. To begin identifying the cellular/molecular mechanisms responsible for this brainstem plasticity, we explored the terminal field organization in adult mice that either received a sodium-replete diet throughout development (controls) or mice fed the sodium-deficient diet from E3-E12. Moreover, we counted the number of ganglion cells, representing the three nerves, recorded whole-nerve neurophysiological taste responses from the CT and IX, and conducted 48hr. 2-bottle preference tests to concentration series of NaCl, sucrose, quinine, and citric acid. Terminal field volumes for each nerve were significantly greater (2X – 4X) in early sodium-restricted mice, and the overlapping zone that received all three nerves was over 15X greater in restricted mice. The differences in terminal fields were accompanied by increased preferences to NaCl and decreased aversions to citric acid, no differences in CT and IX whole-nerve taste responses, and no differences in number of GSP, CT, and IX ganglion cells. We conclude that the early dietary manipulation had a profound effect on early NST development and that the terminal field alterations impacted taste-related behaviors. Acknowledgements: R01 DC00407

#P225 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Renewal Kinetics of Taste Bud Cells in Adult Mice

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Taste bud cells are continuously renewed from a population of progenitor cells, which express cytokeratin (K)5. These progenitors reside outside taste buds and give rise to daughter cells, which exit the cell cycle, enter buds and differentiate into one of 3 taste cell types (I, II, III). Differentiated taste cells live, on average, for 10 days, although variance around this mean is large, suggesting different cell types have different longevities (Beidler & Smallman '65 J Cell Biol 27:263). To explore the idea of cell type-specific lifespans, we employed inducible genetic birthdating, comprising a K5rtTA driver and a tetracycline-inducible reporter allele, which encodes a nucleosomal protein, Histone2B fused with GFP (tetO-H2BGFP, Tumbar et al., 2004 Science 303:359). When K5rtTA;tetO-H2BGFP mice eat doxycycline (dox) chow, K5+ cells produce H2BGFP, which is incorporated into nucleosomes during S phase. Once mice are taken off dox, H2BGFP is no longer transcribed, and the cohort of GFP labeled cells comprises the "pulse". Here, bigenic mice were fed dox chow for 12 hours, and tongues harvested between 3 and 28 days. In the posterior circumvallate papilla, an average of 2 cells/ bud was GFP+ after a 3 day chase. This increased to 4 GFP+ cells/bud by 14 days, and persisted through 21 days post-dox. At 28 days, however, only 2 cells/bud were GFP+. At 14 days, 2 GFP+ cells/bud were PLCß2+ type II cells, whereas on average, less than 1 GFP+ cell/ bud were Snap25+ type III cells. The number of type II cells/bud began to decline at 21 days, while type III cells/bud were fewer by 28 days. We are currently determining if type II cell lifespan is less than that of type III cells, and/or if type III cells are generated less frequently from later divisions of GFP+ K5+ progenitors. Acknowledgements: R01 DC012383 to LAB P30 DC004657 to D. Restrepo

#P226 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Bitter taste similarities among heterozygous MZ twins compared with homozygous MZ twins.

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Heterozygous alleles of select genes are known to be expressed differentially in different individuals. And for some genes, expression in heterozygous monozygotic (MZ) twins is under strong genetic control (twins resemble each other in allele expression, but differ from twin pair to twin pair). The mechanism of action of differential allelic expression is unclear. In order to investigate the potential genetic influence of differential expression of taste genes, we examined the bitter taste phenotypic response of MZ (identical) twin pairs to the bitter tastant 6n -propyl-2-thiouracil (PROP). Volunteers at the Twinsburg Twins Days Festival in Cleveland OH tasted PROP and recorded their perceived bitterness intensity on a generalized labeled magnitude scale (LMS). DNA samples were collected by cheek swab from each subject and were genotyped at *TAS2R38* amino acid codon positions 49, 262, and 296. MZ twins were grouped by their TAS2R38 diplotype. We compared the similarity of Twin A vs Twin B for heterozygous MZ twins to the similarity of Twin A vs Twin B for homozygous MZ twins. The heterozygous MZ group displayed greater perceptual variation between twins than the homozygous MZ group, despite the fact that the homozygous group was comprised of both AVI/AVI and PAV/PAV homozygous subgroups. Thus, to the degree that phenotype reflects expression, it appears that allelic expression of bitter taste receptors is under significant non-genetic control within heterozygous MZ twins. Acknowledgements: Funded in part by NIH DC 02995 to PASB.

#P227 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

TAS2R polymorphisms and the bitterness of RebaudiosideA and RebaudiosideD

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With growing demand for natural non-nutritive sweeteners, extracts from the *Stevia rebaudiana* Bertoni plant have become a popular replacement for sugar. These exacts contain a mixture of various taste active glycosides, with steviol being the most abundant. The second most abundant glycoside is Rebaudioside A (RebA). RebA (>98% pure) is a GRAS (generally recognized as safe) ingredient in the United States, while stevia (the mixed extract) is classified as a dietary supplement. Another glycoside of interest is rebaudioside D (RebD), due to its high dose response for sweetness and minimal bitterness relative to steviol and RebA. Like saccharin and acesulfameK (AceK), the bitterness from stevia glycosides varies across people. Previously, variable saccharin/AceK bitterness has been associated with single nucleotide polymorphisms (SNPs) in bitter receptor genes (*TAS2Rs*). As part of an ongoing study, we explored whether *TAS2R* SNPs may explain variable RebA and RebD bitterness. After a brief orientation with bitter, sweet and metallic training references, participants rated RebA, RebD, aspartame, sucrose, and gentiobiose (a β 1-6 linked disaccharide) for these sensations on a general Labeled Magnitude Scale. Salivary DNA was obtained and genotyped via Sequenom MassARRAY. As expected, mean RebD bitterness was much lower than RebA. In preliminary analyses, RebA bitterness associated with a coding SNP in *TAS2R9* and a synonymous SNP in *TAS2R50*. For the *TAS2R9* Ala187Val SNP, Ala187 allele carriers reported less bitterness than Val187 homozygotes. For RebD, the *TAS2R50* SNP predicted bitterness, although this is likely a tag SNP for another polymorphism given the synonymous substitution. Finally, *TAS2R31* SNPs previously shown to predict AceK and saccharin bitterness did not predict bitterness from RebA or RebD. Acknowledgements: Supported by funds from the Pennsylvania State University and NIH grant DC0010904.

#P228 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

Sucrose analgesia and the cold pressor test in young men: Methodological considerations

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Sucrose is mildly analgesic in infant rats, human neonates, and prepubertal children. This effect generalizes to non-nutritive sweeteners, indicating the effect is due to sweet taste. However, consistent sweet analgesia in adults remains elusive: some studies find an effect while others do not. Pain can be safely induced in the laboratory using the Cold Pressor Test (CPT), providing a convenient means to study this phenomenon. It is unresolved whether the inability to consistently observe analgesic effects in adults is due to methodological issues associated with the CPT or an age dependent effect. White and Prescott (AChemS, 2012) reported strong order effects; tolerance was greater in the second CPT within a session. They suggested rewarming the hand between tests might reduce this bias. Here, we describe 2 studies that attempt to refine an adult sweet analgesia CPT paradigm. In study 1 (36 men), pain was induced by placing the dominant hand in circulating water at 8°C. Within a session, tastants were water and 0.7M sucrose; participants were tested twice (fed / fasted) in a double crossover design. The hand was rewarmed in 35°C water between trials, and hand temperature was confirmed with a laser thermometer. No tastant effect, regardless of hunger state, was observed. However, a weak trend for an order effect within a session was evident, despite rewarming. In study 2 (27 men), subjects received sucrose or water on separate days after an overnight fast. The cold bath was reduced to 4°C, and outcomes included pain threshold (onset in s) and tolerance (hand withdrawl in s). Pain thresholds and tolerance were greater on day 2, but this occurred irrespective of tastant. Collectively, these data suggest increased tolerance in the CPT with repeat exposure is not an effect of initial hand temperature. Acknowledgements: The Pennsylvania State University and USDA Hatch Act funds

#P229 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Are individuals with elevated food liking scores ('foodies') hypergeusic?

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The public believes that foodies are supertasters (and vice versa), consistent with reports that chefs and wine experts report greater bitterness from propylthiouracil (PROP). However, the two reports that test this hypothesis conflict. Minski et al. reported 'high food interest' individuals ('foodies') rated quinine, sodium chloride and PROP as more intense than those with average or low food interest in a laboratory study (n=100), while Pickering et al. failed to find any difference in the bitterness of PROP impregnated discs sent via mail (n>900). These studies also differ in how high food affect individuals were identified: via a ratio of affective ratings for all foods to pleasant non-food item versus a difference score of mean liking for all foods minus mean liking for all non-foods. Here, we explore this question in 246 subjects who completed a generalized hedonic survey (i.e. food & nonfood items) and whole mouth ratings for sucrose, quinine, and PROP. We characterized subjects as high affect using both approaches. Regardless of the categorization method, sucrose, quinine, and PROP intensity ratings did not differ by group in ANOVA. When groups were predicted in logistic regression ('do higher taste ratings predict being a foodie?') there was no evidence supporting this hypothesis. Adding the personality trait Sensation Seeking as a covariate did not alter these conclusions. We did find evidence of lower Sensation Seeking scores among foodies (as defined via the difference score), but further inspection suggests this was due to a small increase in the mean liking of pleasant non-food items when mean food liking was flat. These data fail to support the hypotheses that a) hypergeusic individuals show higher food related affect or that b) higher food affect predicts heightened taste response. Acknowledgements: funds from the Pennsylvania State University and NIH grant DC0010904.

#P230 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Effects of Food Neophobia on Salivary ph, Cortisol and Adrenal Level

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Food neophobics (individuals reluctant to try novel foods) and food neophilics (individuals with an overt willingness to try novel foods) differ in several physiological aspects. Phenylthiocarbamide (PTC) tasting ability, a genetic predisposition, differs among the two groups with more food neophobics possessing this inherited trait. Food neophobics salivate less when presented with novel foods and have higher physiological stress responses to novel foods (increased pulse, GSR, and respirations). The present study assessed salivary pH, adrenal level and cortisol level in food neophobics, food neophilics and an average group, to determine whether such salivary flow and physiological stress reactions could partially be explained by such variables. Salivary mouth swab samples were obtained from 117 participants, who also completed the Food Neophobia Scale (FNS) to assess level of food neophobia. A significant MANCOVA result was found, $F=2.47$, $p=.03$. Further analysis revealed food neophobics had significantly higher levels of salivary cortisol compared to food neophilics and the average group, $F(2,102)=7.53$, $p=.001$. The finding that higher levels of the stress hormone cortisol are present in food neophobic's saliva supports past research indicating a greater physiological stress reaction to novel food stimuli in these individuals. Future research should assess whether exposure to novel foods can decrease the level of salivary cortisol in food neophobics, as a way of promoting a more varied and healthful diet.

#P231 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

The NIH Toolbox Brief Gustation Assessment Protocol

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NIH Toolbox developed standardized, brief assessments for sensory, motor, cognitive and emotional function that are designed for use in longitudinal studies, epidemiological research, and clinical trials. The sensory battery consists of brief assessments of gustation, olfaction, vision, audition, pain, and vestibular balance; all six can be administered within 30 minutes, including 6 minutes for the assessment of gustation. The Gustation Assessment begins with instructions in use of the general Labeled Magnitude Scale by rating of remembered lights (dimly lit restaurant, well-lit room, brightest light ever seen). Four taste trials are then delivered: 1 mM Quinine HCl applied to the anterior tongue, 1 M NaCl applied to the anterior tongue, 1 mM Quinine HCl whole mouth (sip and spit), and 1 M NaCl whole mouth. Rinsing with water is done between trials. As part of the NIH Toolbox national norming study, the Gustation Assessment was given to 1843 English-speakers and 240 Spanish-speakers. These included 494 subjects aged 12 to 15 years and 509 aged 15 to 19 years. For 172 subjects, the battery was given twice to establish test-retest reliability. Preliminary intraclass correlations (ICC) indicate that the test is reliable for whole mouth ratings (ICC = 0.54 for Quinine and 0.57 for NaCl) and reliable for NaCl on the anterior tongue (ICC = 0.42). Quinine ratings for the anterior tongue were less reliable (ICC = 0.29),

but this was always the first trial. For the entire norming sample, small, but statistically significant, declines in taste intensity with age were observed for each of the four trials (Pearson correlations from -0.1 to -0.2, p <0.001). Initial findings indicate that this brief gustation assessment is reliable and sensitive to the gradual decline in taste perception that occurs with age. Acknowledgements: This project was funded by Federal funds from the Blueprint for Neuroscience Research and the Office of Behavioral and Social Sciences Research, National Institutes of Health, under contract number HHS-N-260-2006-00007-C. The National Children's Study also provided support for norming.

#P232 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Establishing Best Practices for an Effective Community-Based Research Laboratory

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The American Association for the Advancement of Science has become a strong advocate for positive and effective dialogue between the scientific and public communities, but recognizes the strengths, weaknesses and limitations that exist towards these efforts. As relayed in the AAAS Public Engagement online video, "Researchers may not be accustomed to such public interaction, but it's crucial to the science/society relationship." Towards this effort, the Denver Museum of Nature & Science established a citizen-scientist run, community-based Genetics of Taste laboratory. In the past three years of active research, we've found that the community-based lab is a unique environment for conducting research in which we are constantly optimizing the balance between providing an enjoyable educational experience and collecting data that is scientifically sound. Here we present the lessons learned in developing a community-based lab and how academic and research institutions can apply this model to their studies. In terms of research study design, involvement of citizen-scientists in the planning process is not only a suggested best practice, but also helps to establish motivation and commitment early in the study. Initial planning should include in-depth discussions of intended outcomes and a clearly defined timeline with tangible milestones to measure progress. Educational outcomes should be included, and care should be taken to have these goals as clearly defined as the research outcomes. Finally, an investment to rigorously train citizen-scientists is a large upfront time commitment for professional staff, but we have found that this investment ensures long term quality control of citizen-science collected and prepared data, which saves resources in the long term. Acknowledgements: 2008-2012 R25 RR025066 NIH NCRR SEPA

#P233 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Carbonic anhydrase CA6 (gustin) polymorphisms and perceived taste intensity

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Polymorphisms in the carbonic anhydrase *CA6* gene (i.e., gustin) reportedly account for additional variation in the bitterness of 6-n-propylthiouracil (PROP) above and beyond that of the TAS2R38 gene. It has been hypothesized that *CA6* influences taste thresholds for and the perceived intensity of PROP via differences in gustin function, and that gustin may be a trophic factor for taste bud development (Calò et al 2011). If true, we reasoned such effects should not be limited to PROP, and should generalize across qualities to other stimuli. As part of an ongoing study, healthy participants (aged 18-45) rated their perception of sweet, sour, salty, savory/umami, bitter, and burning sensations on a generalized Labeled Magnitude Scale for sucrose, sodium chloride, potassium chloride, quinine hydrochloride, PROP, citric acid, capsaicin and a monosodium glutamate/inosine monophosphate (MSG/IMP) mixture. Fungiform papillae density was assessed via digital still microscopy. Salivary DNA was obtained and genotyped using Sequenom MassARRAY. We examined 14 *CA6* SNPs: rs12748400, rs17032907, rs2274327, rs2274328, rs2274333, rs2274334, rs3737665, rs3765964, rs3765965, rs3765967, rs3765968 and rs7545200. We failed to observe differences in sweet, sour, or savory ratings across any of the SNPs tested. Nor were there any differences in FP density for any of the SNPs examined. However, perceived saltiness associated with a number of SNPs in *CA6*. Additionally, FP density was correlated with the intensity of sucrose, PROP and salt, as would be expected. In summary, polymorphisms within *CA6* did not predict overall differences in taste intensity, although salty intensity differed with some *CA6* SNPs. We did not find evidence to support an association between *CA6* SNPs and PROP bitterness that had been reported previously. Acknowledgements: Supported by funds from the Pennsylvania State University and NIH grant DC010904.

#P234 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Taste Detection Threshold in Children

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In light of the unknown relationship between taste perception and obesity in children, the uncertain relationship between sweet taste and obesity, and the overlap of sweet and umami tastes at mechanistic level (e.g., both employ the taste receptor T1R3 in the dimer), the present study, examined the perception of these two taste qualities along with salt (as a control taste) in obese and normal-weight children. To this end, 97 children

were phenotyped for detection thresholds for sweet (sucrose), savory (monosodium glutamate), and salty (NaCl) taste using age-appropriate psychophysical testings, dietary habits, blood pressure and obesity. Preliminary analyses revealed that the detection threshold for sucrose, salt, and MSG are similar to that previously reported in adults and there were no differences observed between normal weight children and obese children in the detection thresholds for any of these basic tastes. In normal-weight, but not obese children, salt detection thresholds were positively correlated with systolic blood pressure. As a group, the greater the waist circumference, the lower the sucrose detection threshold (the more sensitive the child was to sucrose) ($p=0.02$). No such relationships existed for salt or MSG in children. Whether the lower detection thresholds for sucrose are associated with stronger reinforcing value of sweet foods, as has been observed in adults, and understanding the link between salt taste thresholds and blood pressure, are important areas for future research. Acknowledgements: This project was funded by an investigator-initiated grant from Ajinomoto, Inc.

#P235 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Statistical Analysis of Factors Previously Described as Significant in the Ability to Taste Propylthiouracil Yields Roles for Age, Sex and *Tas2r38* Haplotype, but not Fungiform Papillae Density

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The Genetics of Taste research study at the Denver Museum of Nature & Science is in a unique position to collect samples from a diverse population across a wide age range. Using this large population sample we set out to establish the scientific credibility of our community-based laboratory by replicating four previously reported statistically significant factors in the ability to taste propylthiouracil; 1)Age, 2)Sex, 3)*Tas2r38* haplotype, and 4)Fungiform papillae density. Using regression analysis and the Student T-test we can replicate the role of age and sex in taste score (gLMS following a propylthiouracil taste test). Similarly, the presence of at least one dominant allele for the *Tas2r38* gene is a significant predictor of taste. Finally, in order to decrease subjectivity, we developed a dichotomous key for objective analysis of fungiform papillae density. Using this method we did not find that increased papillae density correlates to an increased propylthiouracil taste score. In conclusion, the ability to replicate the significance of age, sex and *Tas2r38* haplotype, as well as the development of objective methodology for papillae analysis, all demonstrate the ability for citizen-scientists in a community-based laboratory to collect, prepare and analyze data that can contribute to the field of chemoreception. In addition, we submit that using standardized methodology for fungiform papillae density allows for a more objective analysis of morphological data. Using this methodology we find no relationship between fungiform papillae density and propylthiouracil score in our data set. This data contradicts previously published studies and suggests that fungiform papillae density may not be as reliable a metric for classifying taster status as previously thought. Acknowledgements: This work was supported by volunteer citizen-scientists at the Denver Museum of Nature & Science, and through support from 2008-2012 from R25 RR025066 NIH NCRR SEPA.

#P236 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

The effects of temperature on sequential and mixture interactions between sucrose and saccharin

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The sweet taste of sucrose and saccharin has been shown to depend on stimulation of the T1R2-T1R3 receptor, but it is also clear that these two stimuli interact with the receptor in different ways. Most recently it was found that self-adaptation is temperature-dependent for sucrose but not for saccharin (Green & Nachtigal, 2012), and a previous study showed that high concentrations of saccharin can block the sweetness of sucrose (and of itself) and evoke a sweet water taste (Galindo-Cusperino et al, 2006). The aim of the present study was to determine if temperature modulates the ability of sucrose to cross-adapt saccharin and/or of saccharin to block the sweetness of sucrose and produce a sweet water taste. Subjects rated the sweetness and bitterness of 0.42 M sucrose, 3.2 mM saccharin, 100 mM saccharin, or binary mixtures of sucrose and the 2 concentrations of saccharin, with and without pre-exposure to themselves or each of the other stimuli. The variables of interest were the duration of pre-exposure (3 or 10 s) and solution temperature (37° or 21°C). The stimuli were sampled by dipping the tongue tip into the solutions, and intensity ratings were made on the gLMS before the tongue was retracted back into the mouth. The results confirmed the previous findings and showed that (1) the magnitude of sweet water taste (after exposure to 100 mM saccharin) is temperature-dependent, and (2) surprisingly, pre-exposure to sucrose for 3 or 10 sec appeared to counteract the ability of 100 mM saccharin to block sweetness, independent of temperature. These results support the hypothesis that sucrose and saccharin bind to at least 2 different sites on the T1R2-T1R3 receptor and raise new questions about the factors that can affect excitatory and inhibitory interactions between these sites. Acknowledgements: Supported in part by NIH grant DC005002

#P237 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

Language Determines Whether Taste Sensitivity is Related to Moral Disgust

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The stimuli that trigger emotional disgust are currently debated. Most contested is whether responses to visceral triggers of disgust (e.g., cockroaches, disease) are fundamentally the same as responses elicited by moral transgressions (e.g., lying, cheating). To address this issue, the present study examined whether: (1) visceral and moral disgust share a common oral origin (the rejection of bitter tasting poisons); (2) verbal priming can alter whether disgust is experienced as a function of taste sensitivity. 102 undergraduates completed a "Behavioral Situations Questionnaire" developed for the present research which compared "grossed out" and "angry" to assess three types of moral transgressions that varied in the degree to which a visceral disgust dimension was invoked (non-visceral, implied visceral, directly visceral), and two standard tests of disgust sensitivity. After completing the questionnaires, taste sensitivity was assessed with a bitter tasting compound (6-*n*-propylthiouracil; PROP). Results showed that the more bitter PROP tasted the more sensitive a participant was to visceral measures of disgust sensitivity, but not to moral disgust sensitivity. There were also no effects for taste sensitivity or type of moral transgression when "angry" was primed for evaluating the transgressions. However, when "grossed out" was primed, the more intense PROP tasted the more "grossed out" participants were by all transgressions, regardless of their visceral nature. This supports the proposition that moral and visceral disgust do not share a common oral origin, but shows that linguistic priming can transform a moral response into a viscerally repulsive event and that susceptibility to this priming varies as a function of an individual's sensitivity to the origins of visceral disgust—bitter taste.

#P238 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

Individual differences in the rate of salivary α-amylase production and its role in the perception of glucose polymers

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Our recent data suggest that some humans can consistently taste glucose polymers, implying possible existence of a glucose polymer receptor. A potential confound of this idea is that the hydrolysis byproducts of the glucose polymers, i.e., glucose and/or maltose, may have, at least to some extent, influenced taste responsiveness of the tasters. The latter scenario is easily rationalized due to the catalytic activity of salivary α-amylase. The present study was designed to investigate (1) individual differences in the rate of α-amylase production and (2) the role that it may play in glucose polymer perception. Measured rate of salivary flow (mg/sec) and α-amylase activity per mg saliva were used to calculate the rate of α-amylase production (activity/sec). The same Ss rated the taste intensity of glucose, sucrose, and glucose polymer solutions (differing in average chain length) following a sip and spit procedure. Results showed large individual differences in the rate of α-amylase production (>30-fold). This can be attributed to the large differences in salivary flow rate (>18-fold) and α-amylase activity (>30-fold). Notably, average rates of α-amylase production were similar between the taster and non-taster groups. Further, within each group, responsiveness to glucose polymers did not appear to differ between individuals with high and low rates of α-amylase production. These findings suggest that salivary α-amylase plays an insignificant role in glucose polymer perception. Alternatively, it is possible that the chain lengths of the glucose polymers tested were too short, i.e., the effect of α-amylase on the hydrolysis was comparable between high and low α-amylase producers. This possibility is currently being explored in a follow-up experiment by using more complex carbohydrates as test stimuli.

#P239 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

Evidence that humans can taste glucose polymers

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Previous findings of behavioral and electrophysiological studies have shown that rodents can taste solutions of Polycose and further can discriminate the taste of Polycose from that of sugars. Recent studies have also shown that the T1R2/T1R3 single and double KO mice respond significantly to Polycose. Based on these data, the possible existence of a glucose polymer receptor has been proposed. In contrast, it has been assumed that glucose polymers are tasteless to humans, although it is known that they evoke a slight odor. During a preliminary study of the role of salivary α-amylase in the perception of glucose polymers, some Ss reported that the glucose polymers had "bread-" or "cereal-like" taste which they could differentiate from the sweet taste of sugars. The current study was therefore designed to measure individual differences in taste perception of various carbohydrates (glucose, sucrose, and glucose polymers of different chain length) and NaCl. Ss rated taste intensity of test solutions while their noses were clamped. The results showed that the perceived intensities of glucose, sucrose, and NaCl were significantly correlated (r=.68~.80, p<.01), but not with the glucose polymers, whereas the intensity ratings of the glucose polymers were highly correlated with one another (r=.62~.86, p<.01). Notably, there was much greater variability across individuals in the responsiveness to the glucose polymers than to the other stimuli. These data provide evidence that some humans can consistently taste glucose polymers of various chain lengths (DE 20-5) and that the reactivity to glucose polymers is independent of that to sugars. The current findings thus support the existence of a secondary carbohydrate receptor in humans that is activated by glucose polymers.

#P240 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

The role of gene expression in the human *TAS2R38* genotype-phenotype relationship

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Bitter taste is important for sensing and avoiding toxins, but the aversion to bitter can lead to low consumption of vegetables, an important source of phytochemicals. Single-nucleotide polymorphisms in the genes that code for the 25 human bitter receptors (*TAS2R*s) result in different individual responses to taste stimuli. One example of this phenomenon is the *TAS2R38* gene, which encodes a receptor that recognizes compounds including 6-*n*-propylthiouracil (PROP) and goitrin, found in broccoli. Cell-based assays and psychophysical threshold measurements confirm that receptor with the amino acid sequence PAV responds to PROP, while the AVI form does not. Heterozygous (PAV/AVI) individuals display a broad range of abilities to taste PROP. To examine the role of allele-specific gene expression in the *TAS2R38* genotype-phenotype relationship we recruited healthy, non-smoking adults with the PAV/AVI diplotype (N=18). Psychophysical ratings for several bitter compounds and vegetable juices were related to levels of *TAS2R* gene expression from human fungiform taste papillae. Increased levels of the PAV form of *TAS2R38* were positively correlated with the subject's intensity ratings for PROP and broccoli juice. Expression of *TAS2R43* was associated with ratings for caffeine, urea, denatonium benzoate and quinine. This relationship resulted from copy number variation of *TAS2R43* and suggests that *TAS2R43* acts as a proxy for bitterness sensitivity from the cluster of receptors on chromosome 12. Our data provide a link between genotype and phenotype in the taste system. Our work lays a foundation for future studies about regulatory mechanisms and implications of taste receptor expression as it relates to diet and vegetable consumption in humans. Acknowledgements: Supported by F32DC011975 (SVL), P30DC011735 (DRR) and R01DC011287 (JAM).

#P241 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Evidence that cooling affects the sweetness of sugars via 2 separate mechanisms.

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Previous experiments in our laboratory demonstrated that temperature can affect the sweetness of sucrose, glucose, and fructose solutions by modulating taste adaptation: Cooling from 37°C to 21°C significantly increased the rate and amount of self-adaptation when the tongue tip was dipped into the solutions for several seconds. However, cooling to 21°C did not reduce initial sweet taste intensity, and thus did not directly affect sensitivity to the sugars. In the present study we investigated whether cooling to colder temperatures would further accelerate sweet taste adaptation and/or begin to reduce sweet taste sensitivity. Subjects rated the sweetness of 0.42 M sucrose solutions at temperatures of 41°, 37°, 30°, 21°, 10° or 5°C after dipping the tongue tip for 0, 3, or 10 sec into either 0.42 M sucrose or pure dH_2O of the same temperature. Sweetness ratings were made prior to retracting the tongue back into the mouth. There were two main findings: (1) sweet taste adaptation increased significantly at 21°C (replicating our previous results), and (2) pre-exposure to pure dH_2O at 5° or 10°C significantly reduced sweet taste intensity independent of taste adaptation. These findings indicate that cooling interferes with the perception of sucrose sweetness in two different ways: mild cooling increases the rate of adaptation whereas more extreme cooling reduces the initial sensitivity to sucrose. Experiments are planned that will test the hypothesis that these two effects occur at different stages of the transduction cascade, with the former affecting the binding of sucrose to the transmembrane region of the T1R2-T1R3 receptor, and the latter modulating a temperature-sensitive intracellular mechanism that is common to G-protein coupled receptors (e.g., TRPM5). Acknowledgements: NIH grant RO1 DC005002

#P242 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

The Chemosensory Component in the 2012 National Health and Nutrition Examination Survey (NHANES): Test-Retest Analysis and Comparison with Laboratory-Based Measures

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The NHANES now includes a standardized chemosensory protocol with brief assessments of taste intensity and odor identification conducted in a mobile exam center. After orientation to the general Labeled Magnitude Scale and scaling intensity of LED-generated lights, participants report intensities of 1 M NaCl and 1 mM quinine hydrochloride applied to the tongue tip and these plus 0.32 M NaCl with the whole mouth. Olfactory dysfunction is assessed with two 4-item, scratch-and-sniff tests (Pocket Tests™ (PT), Sensonics, Inc) with food (strawberry, chocolate, onion, grape) and common (leather, soap, smoke, natural gas) odors. Here we examined test-retest reliabilities of the chemosensory protocol, compared the PT with an olfactometer identification task, and added scaling to all odor tests. Fifty adults (mean age=27, range 18-62 yrs), primarily Caucasian and Asian, college-educated and reportedly healthy, were tested in a laboratory twice within two weeks.

The taste test intraclass correlations (ICC, single measures) ranged from moderate to substantial agreement (0.47 NaCl, 0.50 quinine tongue tip; 0.75 quinine whole mouth). Both PT trials classified 98% of the participants as normosmic. There were good correlations between the individual PT odor intensities (ranging 0.44 for grape to 0.72 for gas) and a moderate overall ICC (0.56). The PT and olfactometer odor intensities were correlated, averaging 0.5 (ranging 0.28 for chocolate to 0.65 for grape). Correct and incorrect odor identification was consistent across the PT and olfactometer tests, averaging 86% agreement. These findings show that, in ideal testing situations, the NHANES protocol had very good reliability and the Pocket Test corresponded reasonably well among normosmics with a measure having more stimulus control. Acknowledgements: NIDCD/NIH

#P243 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Efficacy of sodium and glutamate in reducing bitterness in children and adults

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A central challenge of administering medicine to children is a 'matter of taste' because drugs, by their very nature, often taste unpleasant with bitter taste being the primary culprit. As part of an ongoing study on individual differences in bitter taste perception, we present here preliminary data on ratings of the bitterness of urea and propylthiouracil (PROP) with and without the addition of a sodium gluconate or glutamate (putative blockers) in a racially diverse group of 3- to 10-year old children and adults. Using forced-choice procedures, each child and adult was presented with all possible pairs of the four solutions for each bitter agent (e.g., 0.5M urea, 0.3M sodium gluconate, 0.5 M urea+0.3M sodium gluconate, and water), one pair at a time, and asked to indicate which of the pair tasted more bitter. The data for each bitter stimulus were expressed as the proportion of children or mothers that chose one member of the pair as tasting more bitter and from this, each of the four solutions were ranked according to subject's ratings (1=least bitter; 4=most bitter). Adults also used gLMS to rate taste qualities of each solution in another session. Preliminary analysis revealed that most children (75%) were able to complete the task; the vast majority of those who did not complete the task were of the younger age (<6 years) range, highlighting the difficulty in such assessments of younger children. In adults, we also found that either blocker significantly reduced the gLMS rating of urea bitterness but sodium gluconate was ineffective for blocking the bitterness of PROP. Paired comparison data yielded similar findings in adults as well as children. Acknowledgements: This project was funded by R01DC011287 and supported by P30DC011735 from the National Institute on Deafness and Other Communication Disorders. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIDCD or the National Institutes of Health.

#P244 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Generalization of the effects of Na-cyclamate treatment on sensitivity for sugars, sweeteners, and monosodium glutamate supports a role for T1R3 in experience-induced changes in taste

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Treatment with Na-cyclamate (Na-c) significantly changes human taste sensitivity for the monosaccharides glucose (pyranose) and fructose (furanose) and the structurally different high-intensity sweeteners Na-c, D-tryptophan (D-tryp), and sucralose (sucrl), as well as the umami stimulus monosodium glutamate (MSG). However, sensitivity for the disaccharide sucrose (furanose), and perhaps for the disaccharide maltose (pyranose), remains unchanged (Gonzalez, 2009; Kennedy et al., 2012). Here we conducted further testing with maltose. Subjects rinsed their tongues with 4 mM Na-c or water for 10 sec once a day for 10 days. On day 11 or 12, they tasted a concentration series of maltose, each concentration paired with water, and indicated which of each pair was "the sweetener." Subjects treated with Na-c showed increased sensitivity for maltose ($p=0.004$). With respect to the high-intensity sweeteners, responses to Na-c and sucralose are increased by Na-c treatment while responses to D-tryptophan are decreased. Because responses to MSG also are decreased after Na-c treatment, the effect may be different for amino acid stimuli. Testing with the amino acid sweetener aspartame is in progress. Human psychophysical and animal neurophysiology data suggest peripheral mechanisms (Faurion et al., 2002; Hassan et al., 2006; Gonzalez et al, 2009). We have suggested that binding of the treatment compound with the receptor subunit T1R3 leads to changes in binding or other steps in the receptor response to the test compound. Our results show that the mechanism(s) for the changes affect(s) stimulation by various sweeteners differently. The generalization of effects supports our hypothesis that sweet compound interaction with T1R3 leads to changes in the overall receptor response. Acknowledgements: Supported by NIH NIDCD R15DC009042 to LMK.

#P245 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

Glutamate Detection Thresholds Are Altered by the Addition of 5'-Ribonucleotides

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Umami taste intensity of glutamate is synergistically increased in humans by the addition of inosine 5'-monophosphate (IMP) disodium salt and guanosine 5'-monophosphate (GMP) disodium salt, two purinergic ribonucleotides. We hypothesized that the addition of these and other ribonucleotides would decrease the absolute detection threshold of L-glutamic acid potassium salt (MPG) when in admixture; thus, sensitivity to glutamate would be increased. We first measured the absolute threshold to MPG and compared this to the threshold for MPG in the presence of a constant background level of ribonucleotide (3 mM). All thresholds were measured twice in all subjects. We found the additions of inosine monophosphate (IMP), guanosine monophosphate (GMP), and adenosine monophosphate (AMP), lowered the MPG threshold for every subject and were statistically significant $p < 0.001$. Uridine monophosphate (UMP) yielded mixed results that were not significant. Interestingly, cytosine monophosphate (CMP) raised glutamate thresholds in 6 of 10 subjects, suggesting it is an inhibitor of glutamate taste in humans. The average detection threshold of MPG was 1.75^{-03} and with the addition of IMP, the most robust enhancer, the threshold was decreased by approximately two orders of magnitude to 4.46^{-05}. CMP increased the MPG threshold by approximately ten fold in the subject for whom it was most inhibitory. The rank order of effect on increasing sensitivity to glutamate was IMP > GMP> AMP >> UMP // CMP. We will explore associations among perceptual differences in synergistic effects of various ribonucleotides with genetic variations in individual oral glutamate receptors. Acknowledgements: Funded in part by NIH DC 02995 to PASB.

#P246 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

Transient top-down modulation of gustatory sensitivity in humans

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Perceptual systems are dynamic. Sensitivity may decrease due to adaptation or increase as a result of directed attention. In three studies we tested the hypothesis that sustained directed attention to oral stimulation would influence gustatory sensitivity. In study one, six subjects rated the intensity of taste stimuli (sucrose, sucralose, citric acid, sodium chloride, monosodium glutamate) three times before and after they performed a triangle task requiring sustained directed attention to oral sensation. In the triangle test subjects were presented with two qualitatively similar flavor stimuli and asked to "pick the odd one out". They repeated this task 12 times and then rated the intensity of the taste stimuli again. Subjects returned to the lab four times and repeated this procedure. As predicted, taste stimuli were rated as more intense post- vs. pre- triangle test ($p = .009$). However, the effect was transient in that taste stimuli were rated as less intense during the pre-triangle test vs. the previous days' post-triangle test ($p = .000$). In study two we replicated these findings with a sample of 9 subjects ($p = .000$ and $p = .037$). In study three we tested whether consumption of the flavor stimuli without the performance of the triangle test would result in sensitivity changes. Consistent with the hypothesis that it is the performance of the discrimination task, rather than mere exposure to flavors that produces the increased sensitivity to taste, no significant increases in taste intensity were observed post- vs. pre- exposure ($p = .115$). These results demonstrate that performing a difficult chemosensory task results in a transient increase in taste sensitivity, which we suggest reflects a temporary effect of top-down modulation on increasing the efficiency of central taste processing. Acknowledgements: Supported by NIDCD grant R01 DC006706

#P247 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

The Role of Glutamate in Infant Satiation: a Model System

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We recently discovered that human infants consumed less to satiation when feeding formulas high in free glutamate (extensively protein hydrolysate formulas; ePHF) than when consuming a formula low in free glutamate, such as standard cows' milk formulas (CMF). The purpose of this study was to use this model system to characterize the timing and patterning of cues infants use to signal satiation. In this within-subjects study, 41 infants <4 months of age were tested on two separate days under infant-led feeding conditions. In counterbalanced order, infants were videotaped as they fed CMF on one test day and CMF with added free glutamate (CMF+glu) comparable to levels found in ePHF on the other. Raters blinded to the conditions coded the timing and frequency of a variety of behavioral cues and determined the duration of feeding. The infants consumed significantly less formula to satiation and tended to spend less time feeding CMF+glu than CMF. Preliminary analyses revealed that while there were no differences in the types and frequencies of behaviors exhibited between feeds, infants displayed satiety behaviors earlier when feeding the CMF+glu formula compared to the CMF. In sum, we have identified a model system to experimentally manipulate and study infant satiation, an area of research that is needed both for practical concerns of optimizing infant feeding and for theoretical concerns focusing on understanding mechanisms underlying hunger, satiation and satiety. Acknowledgements: Supported by Grants R01HD37119 and HD072307 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, a National Research Service Award F32HD063343 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and an investigator-initiated grant from Ajinomoto, Inc. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The funding agencies had no role in the design and conduct of the study in the collection, analysis, and interpretation of the data or in the preparation, or review of the abstract.

#P248 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

Identification of Neurogenetic Networks that Contribute to Natural Variation in Olfactory Behavior in *Drosophila melanogaster*

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Despite major advances in the identification and characterization of odorant receptors, little remains known about the genetic basis of individual variation in olfactory perception. This issue can be addressed in *Drosophila melanogaster*, where olfactory behavior can be easily quantified for large numbers of genetically identical individuals reared under controlled conditions. We used 168 fully sequenced, inbred, wild-derived lines from the *Drosophila melanogaster* Genetic Reference Panel (DGRP) to perform three complementary genome wide association (GWA) studies to identify alleles that affect natural variation in olfactory behavior to benzaldehyde. First, we performed a GWA on DGRP lines to identify top SNPs associated with mean differences in olfactory behavior. Second, we intercrossed two divergent DGRP lines and constructed an outbred advanced intercross line population, on which we performed an extreme quantitative trait locus GWA. Finally, we performed a GWA for SNPs affecting the variance among lines as a one-dimensional screen for interacting loci, since there is evidence for epistasis between mutations affecting olfactory behavior and mutational effects are suppressed in DGRP line genetic backgrounds. We find that different elements of the genetic architecture that underlies natural variation in olfactory behavior are revealed in the three GWA analyses, but they converge on similar cellular processes and could be functionally validated at a high rate through analysis of mutants. Our results indicate that polymorphisms that contribute to natural variation in olfactory perception are not restricted to the chemosensory sub-genome, but that variation in neural connectivity and synaptic signaling in the central nervous system is a major determinant of individual variation in odor perception. Acknowledgements: This work was supported by National Institutes of Health grants GM59469 and GM45146.

#P249 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

Re-Engineering of Olfactory Receptor OlfCc1 Toward Directed Ligand Selectivity

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Fish sense food cues in their aqueous environment using family C GPCR olfactory receptors. These C family receptors are characterized by a large N-terminal "Venus flytrap" domain. Zebrafish olfactory receptor OlfCc1 is a broadly-expressed ortholog of mammalian V2R2, which shares sequence similarity with the human Calcium-sensing Receptor (CaSR). C family receptors are predicted to respond to amino acids, as do the previously identified OlfCa1 and CaSR. The expression of OlfCc1 in the entire microvillous olfactory neuron population in the zebrafish, as well as its sequence homology with CaSR, make it an interesting target for de-orphaning and engineering, as it could play a generalized behavioral role in zebrafish chemosensation. *In silico* modeling of OlfCc1 identified the receptor's binding pocket and residues likely to be directly involved in ligand binding. OlfCc1 was then cloned into a CMVI FLAG-tagged expression vector and expressed in HEK293 cells. Calcium imaging performed on these cells using Fluo-4 calcium-sensitive dye revealed the calcium-dependent binding profile of OlfCc1, which includes amino acids. Amino acid point mutations were then introduced to OlfCc1, with the aim of broadening the receptor's binding specificity. These mutations succeeded in altering the sensitivity and specificity of OlfCc1 in accordance with predictions. In conclusion, the binding specificity and sensitivity of OlfCc1 can be selectively engineered. Additionally, the combination of *in silico* homology modeling and calcium imaging that constitute this method can be applied to other C family GPCRs, to directly engineer ligand binding capability. Acknowledgements: NSF GRFP and the NIH

#P250 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

Interactions at the olfactory receptor level contribute to the coding of odorant mixtures

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Numerous studies reported that the perceptual characteristics of odorant mixtures are often different from those of their individual compounds; e.g. the mixture intensity can be higher or lower than the arithmetic sum of each component's intensity. These findings raise the question how odorants in mixtures are detected and encoded at the peripheral level of the olfactory system. We investigated this question through the measurement of human olfactory receptor (OR) responses to two specific binary mixtures of aldehydes: (i) octanal and citronellal, known to induce a configural perception in rats (Kay *et al.,* 2003) and masking effects in humans (Burseg *et al.,* 2009); (ii) octanal and methional, known to induce masking effects in humans (Burseg *et al.,* 2009). We used a heterologous expression system (HEK293T cells) in which OR (OR1G1, OR52D1, OR2W1 and OR1A1) were transfected transiently. Responses of OR to odorants applied alone or in mixtures were measured by calcium imaging. The results showed various interactions at the OR level. When octanal was mixed with citronellal, the OR response intensity was reduced thus showing subtraction, compromise or partial addition, depending on the OR and the concentrations of odorants. Interestingly, the mixture of octanal and methional was found to induce mostly synergy, whatever the OR. These data strengthen the hypothesis that interactions can occur at the OR level and could therefore contribute significantly to the olfactory coding of odorant mixtures. Acknowledgements: This work is funded by the National Institute of Agricultural Research and the region of Burgundy

#P251 POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT

Class-specific regulation of a zebrafish olfactory receptor gene

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Olfactory sensory neurons (OSNs) typically express a single allele of a single olfactory receptor (OR) gene from a much larger genomic repertoire; a phenomenon that is not well understood. Experimental evidence suggests that OR expression is controlled by a combination of long- and short-range regulatory sequences. We used promoter bashing in transgenic zebrafish to identify proximal regulatory sites within the OR101-1 gene promoter. Positive regulatory sites are located within the first 500 bp upstream of the transcription start site, while more distant sequences confer a repressive effect on transgene expression, even in the presence of strong genomic enhancers. Interestingly, the

repressive sequence contains binding sites for the transcriptional repressor zbtb7b, which is abundantly expressed in the peripheral zebrafish olfactory system. Preliminary results suggest that negative regulation confers a higher specificity of transgene expression to ciliated OSNs. A major distinction within the OR repertoire can be made between evolutionary ancient class I ORs and the group of class II receptors, which massively expanded in the tetrapod lineage. OR101-1 appears to be the only class II OR in zebrafish. OSNs that fail to express a functional OR usually undergo a second OR gene choice resulting in heterogeneity of OR expression and widespread axonal projection of transgenic OSN axons to olfactory bulb glomeruli. Transgenic OSNs expressing a deletion allele of the OR101-1 gene in contrast target a single specific glomerulus, in the zebrafish olfactory bulb suggesting that second OR gene choice is severely restricted in those OSNs. The results imply that distinct regulatory mechanisms evolved concomitantly with the appearance of the first class II OR in the teleost lineage. Acknowledgements: TÜBITAK, The Scientific and Technological Research Council of Turkey, Grant Awards: 107T760, 112T168

#P252 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Olfactory Receptor (OR) switching is influenced by genome position in olfactory-placode (OP)-derived cells.

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We previously characterized olfactory receptor (OR) expression in the OP6 and OP27 cell lines and made two general observations: OR choice is not a heritable property; and the range of OR representation in OP populations appears biased for a subset of the full OR repertoire. We used custom arrays and deep sequencing to analyze the complete expressed OR repertoire in OP cultures. OP6 and OP27 cell lines have significant overlap in OR representation, consistent with similar pre-specification of the two founder cells, which had been isolated from a common developmental milieu. However, OR representation in OP cultures is not constrained by presumptive expression zones within mouse olfactory epithelium, as might be predicted if the range of OR choices had been pre-specified by developmental (i.e., spatial) cues. Instead, we find strong evidence for 'position-effects': neighboring OR genes are significantly over-represented in divergent populations, suggesting a tendency to switch within versus across OR clusters. Surprisingly, we do not observe differences in common epigenetic marks between "active" versus "inactive" ORs, nor does locus positioning relative to nuclear chromocenters appear to be predictive of selection probability. We suggest a switching model in which the epigenetic microenvironment established by previous OR transcription increases the likelihood of selection/re-selection within that genome region. We hypothesize that the OP6 and OP27 founder cells had been similarly specified, initially leading to a similar bias for OR switching, but that in the absence of further developmental cues during subsequent culturing, probabilistic switching histories have resulted in slow evolution from initial biases, thus independently evolving OR subrepertoires. Acknowledgements: NIH R01-DC006267 NSF 0842868

#P253 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Blockade of Insect Odorant Receptor Currents by Amiloride Derivatives

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Insect odorant receptors (ORs) function as heteromeric odorant-gated ion channels consisting of a conserved coreceptor, Orco, and an odorant-sensitive tuning subunit. Although some OR modulators have been identified, an extended library of pharmacological tools is currently lacking and would aid in furthering our understanding of insect OR complexes. Using whole-cell patch clamp techniques, we demonstrate that amiloride and several derivatives, which have been extensively used as blockers for various ion channels and transporters, also block odorant-gated currents from two OR complexes from the malaria vector mosquito Anopheles gambiae, AgOr48 + AgOrco and AgOr65 + AgOrco. In addition, currents from both heteromeric OR complexes were susceptible to HMA blockade when activated by VUAA1, an agonist that targets the Orco channel subunit. HMA was also capable of blocking VUAA1-evoked currents of Orco homomers from 4 different insect orders, demonstrating that HMA blockade is not unique to AgOR complexes. Additionally, amiloride derivatives have provided insights into the properties of both the channel pore and spontaneous gating across different insect OR complexes. Amiloride derivatives therefore represent a valuable class of channel blockers that can be used to further investigate the pharmacological and biophysical properties of insect OR function. Acknowledgements: This work was supported by the National Institute of Allergy and Infectious Disease [AI056402] to L.J.Z and the National Institute on Deafness and Other Communication Disorders (NIDCD) [DC001655] to B.W.A. at the National Institutes of Health, and the Foundation for the National Institutes of Health through the Grand Challenges in Global Health Initiative [VCTR121] to L.J.Z. G.M.P was supported by the NIDCD through an NRSA F31 [DC011989].

#P254 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Functional Analysis Of Nematode GPCRS In Yeast

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The yeast *Saccharomyces cerevisiae* has been used extensively for ligand screening of human G-protein coupled receptors, due to its ease of genetic manipulation, low cost, rapid growth, and eukaryotic secretory pathway. Although the *Caenorhabditis elegans* genome was sequenced 13 years ago and encodes over 1,000 GPCRs, of which several hundred are believed to respond to volatile organic ligands, only one of these receptors, ODR-10, has been linked to a volatile ligand, 2,3-butanedione. ODR-3 is a G-protein α subunit believed to be involved in odorant detection and activated by ODR-10. Here we report the functional coupling of ODR-10 to the yeast pheromone signalling pathway using the yeast - *C. elegans* chimaeric Gα subunit (GPA-1:ODR-3). Interactions between ODR-10, ODR-3 and the chimaera were confirmed using the split ubiquitin yeast two-hybrid system. We also report the tailoring of a *Saccharomyces cerevisiae* strain for the analysis of *C. elegans* chemoreceptor function. In this study, a yeast *gpa1D ste2D sst2D far1D* quadruple mutant strain was constructed to efficiently couple nematode olfactory receptors with the yeast signalling pathway. We used two different reporters: green fluorescent protein and ß-galactosidase, to verify activation of the signal transduction pathway by ligand activated GPCR interactions. With this heterologously engineered yeast system, we aim to accelerate the de-orphaning of *C. elegans* GPCR proteins.

#P255 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Differentiating activation of intracellular signaling pathways using calcium dynamics

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Mammalian olfactory receptors (ORs) appear to have the capacity to couple to multiple G protein-coupled signaling pathways, more specifically phosphoinositide-dependent signaling in addition to canonical cAMP-dependent signaling, in a ligand-selective manner. To better understand the mechanisms and molecular range of such ligand selectivity, we developed a heterologous expression system with differential readout of intracellular calcium changes. We expressed the mouse eugenol receptor (mOREG) in HEK293T cells together with Gα15 [phospholipase-C (PLC) pathway] and/or Gαolf [adenylate cyclase (AC) pathway], leading to intracellular calcium release or calcium influx through a cyclic nucleotide-gated channel mutant deficient in Ca-CaM negative feedback, respectively. Eleven known mOREG agonists were tested, including eugenol, its analogs, and structurally dissimilar compounds (mousse cristal, nootkatone, orivone). PLC-dependent responses differed dynamically [e.g., eugenol (τ_{rise} = 3.55 ± 0.13 sec; τ_{decay} = 72.42 ± 19.01 sec) from AC-dependent responses (τ_{rise} = 90.83 ± 9.67 sec; τ_{decay} = 167.15 ± 6.18 sec)], allowing them to be distinguished when Gα15 and Gαolf were co-expressed. This difference persisted across ligand concentration. All agonists tested activated both pathways [e.g., EC_{50}, eugenol: 76 ± 12 μM (PLC), 78 ± 26 μM (AC)], showing that mOREG can couple to different G proteins expressed in the same cell. A larger scale screening is under way to identify and characterize potential OR-ligand combinations that differentially activate downstream signaling pathways. Acknowledgements: NIDCD DC001655, DC005995

#P256 **POSTER SESSION V: HUMAN TASTE PSYCHOPHYSICS; OLFACTION RECEPTORS; TASTE DEVELOPMENT**

Profiling of OR gene expression in the human olfactory epithelium

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Background: Olfactory recognition is mediated by a large repertoire of olfactory receptors (ORs). The human genome contains 851 OR loci. More than 50% of the loci are annotated as nonfunctional due to frame-disrupting mutations. Furthermore some missense haplotypic alleles can be nonfunctional due to a substitution of key amino acids governing protein folding or interaction with signal transduction components. Beyond their role in odor recognition, functional ORs are also required for a proper targeting of olfactory neuron axons to their corresponding glomeruli in the olfactory bulb *(Feinstein et al, 2004).* Therefore, profiling of OR gene expression in the olfactory epithelium provides an opportunity to select frequently expressed and potentially functional ORs for large deorphanization campaign. **Methods:** An AB TaqMan® Low Density Array (TLDA) containing probes for 356 predicted OR loci was designed to investigate the chemosensory receptor gene expression in olfactory epithelium tissues from 8 individuals. Total RNA isolation, DNase treatment, RNA integrity evaluation and reverse transcription in cDNA were performed for these 8 samples. Then 384 gene targets (including reference genes for normalization) were analysed using the same RT-qPCR platform. **Results:** The expression of 200 (56%) human OR genes was observed in these olfactory epithelia, among which 114 were robustly expressed in all tested individuals. No relation between OR gene expression and age or sex was observed. Most of the ORs (>80%) deorphanised at Chemcom or described in the literature were found in the expressed set.

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REGISTRATION
7:00 am to 1:00 pm, 6:30 pm to 7:30 pm

WEDNESDAY, APRIL 17

THURSDAY, APRIL 18

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POSTER SESSION I: Multimodal Reception; Chemosensation and Disease; Olfaction Periphery
8:00 am - 12:00 pm
Huntington Ballroom

SYMPOSIUM: THE STRUCTURAL Basis of Chemosensory Signaling
9:00 am - 11:15 am
Grand Ballroom Salon D

REFRESHMENTS AVAILABLE
10:00 am - 10:30 am
Grand Ballroom Foyer

ACHEMS EXECUTIVE COMMITTEE MEETING
12:00 pm - 3:30 pm
Vista Ballroom

INDUSTRY SYMPOSIUM: Taste and Smell in Translation: Applications from Basic Research
1:00 pm - 4:10 pm
Grand Ballroom Salon D

REFRESHMENTS AVAILABLE
2:15 pm - 2:30 pm
Grand Ballroom Foyer

THE BARRY DAVIS WORKSHOP: Federal Funding Opportunities for the New Investigator
3:00 pm - 5:00 pm
Grand Ballroom Salon C

INDUSTRY RECEPTION (Ticketed Event)
4:15 pm - 6:00 pm
Lighthouse Courtyard

WELCOME/AWARDS CEREMONY
5:00 pm - 5:45 pm
Grand Ballroom Salon D

GIVAUDAN LECTURE:
5:45 pm - 7:00 pm
Grand Ballroom Salon D

REFRESHMENTS AVAILABLE
7:30 pm - 8:00 pm
Grand Ballroom Foyer

PRESIDENTIAL SYMPOSIUM: Gut Peptide Interactions Between Taste, Feeding, and Reward
7:30 pm - 9:30 pm
Grand Ballroom Salon D

POSTER SESSION II: Olfaction Development; Taste CNS; Neuroimaging; Olfaction CNS
7:00 pm - 11:00 pm
Huntington Ballroom

Visual Program-at-a-Glance, *continued*

Posters listed for AM and PM Sessions are displayed all day long.

FRIDAY, APRIL 19

REGISTRATION
7:30 am to 12:30 pm, 7:00 pm to 8:00 pm

POSTER SESSION III: Trigeminal; Human Olfactory Psychophysics; Taste Periphery
8:00 am - 12:00 pm
Huntington Ballroom

REFRESHMENTS AVAILABLE
9:30 am - 10:00 am
Grand Ballroom Foyer

PLATFORM PRESENTATIONS: Olfaction
8:00 am - 9:30 am
Grand Ballroom Salon D

SYMPOSIUM: Stem and Progenitor Cells for Taste Buds — Development and Renewal
10:00 am - 12:15 pm
Grand Ballroom Salon D

ACHEMS BUSINESS MEETING
1:00 pm - 2:00 pm
Grand Ballroom Salon D

REFRESHMENTS AVAILABLE
2:15 pm - 2:45 pm
Grand Ballroom Foyer

PLATFORM PRESENTATIONS: Polak Young Investigator Award Winners
2:30 pm - 4:05 pm
Grand Ballroom Salon D

CHEMOSENSORY ENTERPRISE AND MENTORSHIP ALLIANCE (ChEMA) SOCIAL
5:00 pm - 7:00 pm
Lighthouse Courtyard

REFRESHMENTS AVAILABLE
7:30 pm - 8:00 pm
Grand Ballroom Foyer

SYMPOSIUM: New Approaches to Physiology and Behavior in Awake Rodents
8:00 pm - 10:20 pm
Grand Ballroom Salon D

POSTER SESSION IV: Chemical Signaling and Behavior; Animal Behavior/ Psychophysics; Chemosensation and Metabolism; Vomeronsasal and Chemical Communication
7:00 pm - 11:00 pm
Huntington Ballroom

SATURDAY, APRIL 20

REGISTRATION
7:30 a.m. to 12:15 p.m., 5:45 p.m. to 6:15 p.m.

POSTER SESSION V: Human Taste Psychophysics; Olfaction Receptors; Taste Development
8:00 am - 12:00 pm
Huntington Ballroom

PLATFORM PRESENTATIONS: Taste
8:00 am - 9:45 am
Grand Ballroom Salon D

REFRESHMENTS AVAILABLE
9:30 am - 10:00 am
Grand Ballroom Foyer

SYMPOSIUM: Experience Driven Plasticity for the Olfactory System
10:00 am - 12:15 pm
Grand Ballroom Salon D

CLINICAL LUNCHEON (Ticketed Event) — Taste Receptors in Gut and Pancreas Regulate Endocrine Function
12:30 pm - 2:30 pm
Vista Ballroom

SYMPOSIUM: The New 'Faces' of Chemosensation — Utilizing Chemosensory Signaling Pathways Outside the Canonical Chemosensory Organs
3:00 pm - 5:15 pm
Grand Ballroom Salon D

IFF LECTURE: Bitter Taste in Mice and Man
6:15 pm - 7:00 pm
Grand Ballroom Salon D

CLOSING BANQUET (Ticketed Event)
7:00 pm - 9:00 pm
Lighthouse Courtyard

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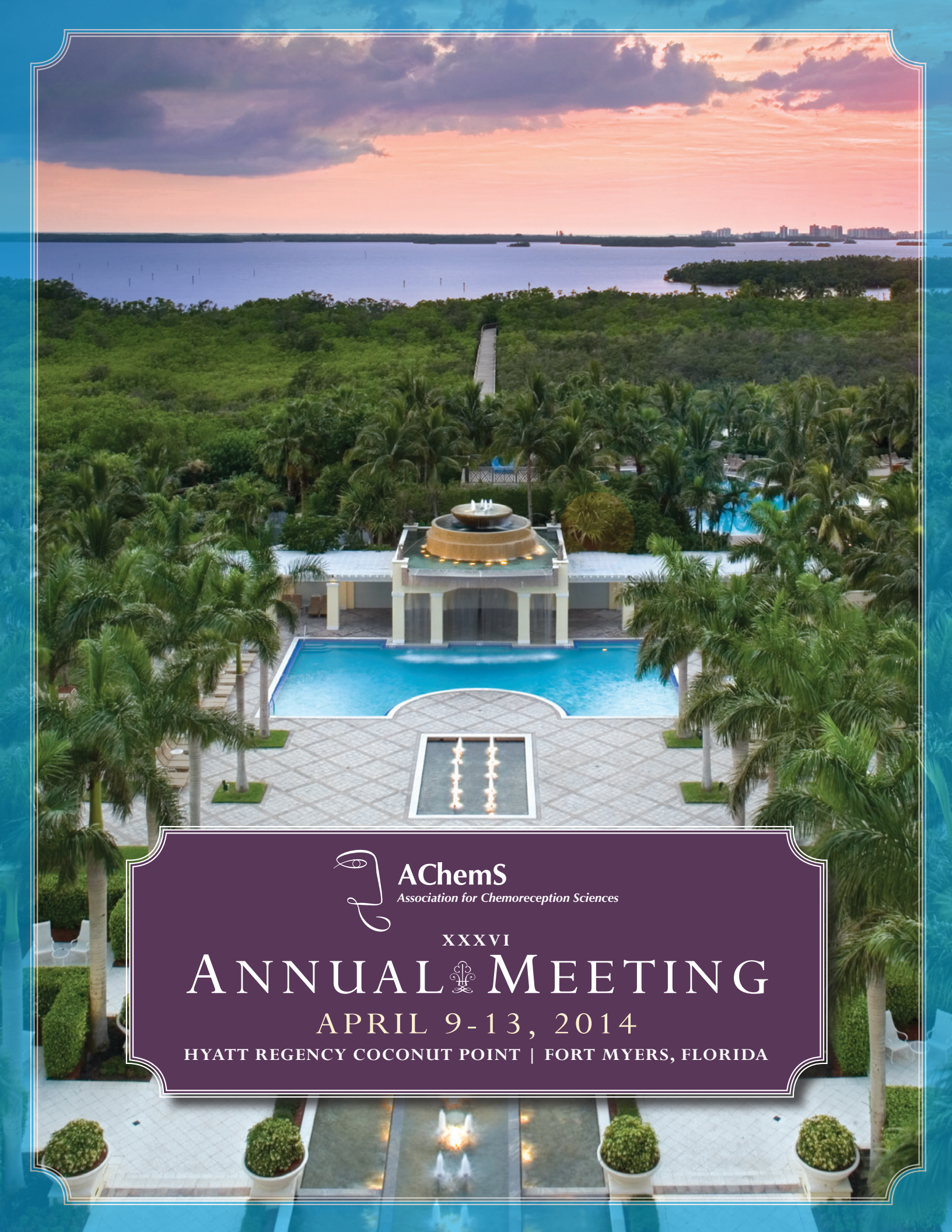

AChemS
Association for Chemoreception Sciences

XXXVI

ANNUAL MEETING

APRIL 9-13, 2014

HYATT REGENCY COCONUT POINT | FORT MYERS, FLORIDA

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