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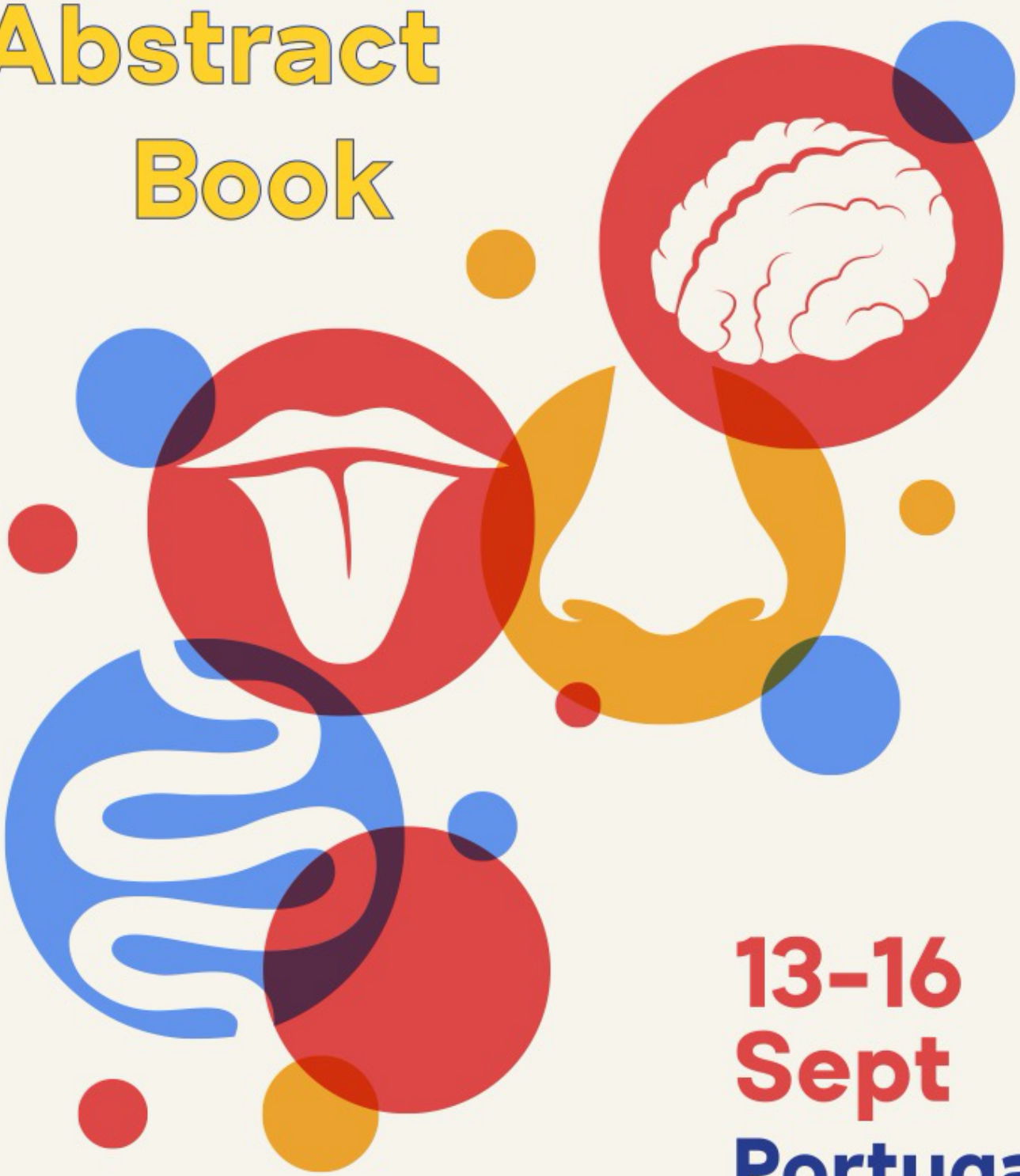

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Mon, 13 Sep -14:00 - 15:30

Satellite Symposium 1 - Pre-Symposium

Mon-PS1-001

Human communication of sickness cues

Mats Olsson

Karolinska Institutet

Contagious diseases have been a fatal threat to humans throughout evolution. Arguably it would serve us well if we were able to learn, with high sensitivity detect, and (when appropriate) avoid sources of contagion. The nature and potency of such a behavioral defense has gained increasing interest during the last decade and is often referred to as the “behavioral immune system”. Humans ability to detect disease cues of different sorts has been of particular interest since this is the basis of a cost-efficient behavioral avoidance of pathogens. Another part of a behavioral defense is the preparatory response of the immune system itself upon the detection of disease cues. This presentation reviews our studies on sickness detection, primarily using an experimental sickness model but also natural diseases. Results indicate that already within hours of the induction of systemic inflammation by way of endotoxin human participants can detect several olfactory, visual (facial and motion) and vocal cues of sickness, which can also be integrated for a better discrimination between healthy and sick people.

Mon-PS1-002

Reutilizing Sweat Samples: The robustness of information transfer through fear chemosignals

Nuno Gomes [1], Fábio Silva [2], Gün R. Semin [1, 3]

[1] William James Center for Research, ISPA - Instituto Universitário, Lisboa, Portugal, [2] William James Center for Research, Universidade de Aveiro, Aveiro, Portugal, [3] Faculty of Social and Behavioral Sciences, Utrecht University, Utrecht, the Netherlands

A considerable volume of research has been showing that human sweat (chemosignals) conveys information about the emotional state of its donor, triggering in receivers congruent psychophysiological and behavioral reactions. For instance, exposure to sweat produced in fear-inducing contexts results in increased activity of the medial frontalis and corrugator supercilii (facial electromyography; fEMG) – two facial muscles involved in fear facial expressions. Nevertheless, despite the increased interest in emotional chemosignals, little is known about the properties of sweat samples. In this study, our goal was to examine whether sweat samples used a second time would produce similar results to their first application. Specifically, we assessed whether sweat samples collected from Portuguese males in fear (vs. neutral) inducing contexts produce similar fEMG activations (i.e., in the medial frontalis and corrugator supercilii) in female receivers across two independent applications (the first with Dutch and the second, a year later, with Portuguese receivers). Our findings showed that exposure to fear (vs. neutral) chemosignals resulted in higher activations of both muscles compared to neutral odors, revealing a similar data pattern across both applications. These results underline the feasibility of re-using emotional (fear) sweat samples (with its obvious monetary and time benefits). Additionally, this similar data pattern provides some insights regarding the properties of the fear-related information present in the samples: Samples reused a year later (conserved at -80ºC) produced a similar data pattern to their first application indicating that the information transfer through (fear) chemosignals appears to be robust and may rely on low volatile molecules.

Mon-PS1-003

Identifying the smell of fear: Psychological experiments, chemical analysis, and genetics

Jasper de Groot

Behavioural Science Institute,Radboud University,Nijmegen,the Netherlands, Utrecht University, Utrecht, the Netherlands

The question of whether human smells can influence our social lives is ranked among the 125 most compelling multidisciplinary scientific challenges of this century. Sensory testing has already shown excellent human smell skills, including social communication. There is abundant psychological and neural evidence for the chemical communication of fear, mainly from Western Caucasian samples. Because it is still unclear which molecules are primarily driving this effect, we combined psychological experiments with a chemical analytical approach (GC-MS). To test generalizability, we examined effects of a single- nucleotide polymorphism (SNP) 538G → A on the ABCC11 gene known to reduce body odor found in only 0-3% of Western Caucasians. First, we effectively induced a fearful and neutral state in two groups of senders (N = 36: ABCC11-AA vs. ABCC11-GG/GA) based on subjective experience and galvanic skin responses. By using part of the samples for

chemical analysis and the remainder for a psychological study that employed a face morph classification task, we could map the chemically identified compounds on receivers' responses. The combined results indicate that the "non-odorous" ABCC11-gene variant AA does not abolish the capacity to chemically communicate fear, leaving open the possibility of a species-wide fear odor. This research was supported by a Veni Innovational Research grant (NWO-016.Veni.195.116) awarded to J.H.B. de Groot.

Mon-PS1-004

The role of olfaction in social communication and wellbeing: The case of autism spectrum

Filipa Barros [1, 2], **Sandra Soares** [1]

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Olfaction plays a crucial role in wellbeing and survival. Humans are able to detect and respond to a vast set of olfactory stimuli, coming from different sources. These are informative about the available resources and threats in the environment, while also playing a role in social communication. In fact, human chemosignals communicate critical information about us and our conspecifics, such as the emotional state, modulating social perception and behaviour. On the other hand, common odours (i.e., non-social odours) are also able to influence the way we perceive and interact with the social world. Despite its role in social perception and functioning, olfactory processing is still underexplored in comparison with other sensory modalities, even in conditions where social cognition is altered – as it is the case of Autism Spectrum Disorders (ASD). In fact, although some studies have explored olfactory perception in the autism spectrum, the literature is still scarce and/or inconsistent. Furthermore, little is known about the relationship between the expression of autism traits in the general population, associated with distinct features of autism (such as social skills or attention to detail), and olfactory perception. In order to extend the knowledge in the field, we will present the results of a set of studies aiming: 1) to review the available evidence about olfactory perception in ASD and the potential of olfactory cues to be social facilitators in this condition; and 2) to explore the relationship between autism and distinct dimensions of olfactory perception. This research was supported by National Funds through the Portuguese Foundation for Science and Technology (FCT – Fundação para a Ciência e a Tecnologia), within the William James Center for Research (UIDB/04810/2020); the CINTESIS R&D Unit (UID/IC/4255/2020); and a Doctoral Grant with the ref. SFRH/BD/118244/2016, granted to Filipa Barros.

Mon-PS1-005

The effect of diet on human body odour quality

Jitka Třebická Fialová, Jan Havlíček

Faculty of Science, Charles University, Prague, Czech Republic

The human body odour is individually specific and relatively stable due to its genetic bases. However, numerous factors affect its hedonic quality, such as hormonal changes, affective states, diseases, and diet, which is often considered the most significant source of variation. The body odour can be influenced directly by specific aromatic compounds or their metabolites from the diet and indirectly by diet quality and food deprivation. Numerous volatile compounds may emanate in breath odour or, after being metabolized by the digestive system, can affect the axillary odour, odour of urine, faeces, amniotic fluid, breast milk, and mother's diet even the body odour of her newborn baby. The effect of diet on human body odour quality will be illustrated in several our studies that showed, for example, that red meat consumption negatively affects hedonic valence of body odour, while garlic consumption and restoration of caloric intake after food deprivation has positive effects. Mechanisms of odour changes include direct excretion of specific chemicals or metabolites directly derived from the diet or more complex pathways, especially in the case of skin glands where chemicals from the diet are usually transported via the bloodstream and might be metabolized further in the liver. However, for most substances, mechanisms and metabolic pathways of such changes are not known, and more empirical work in this fascinating area of chemical communication is needed.

Mon, 13 Sep -16:00 - 17:30

Satellite Symposium 2 - Pre-Symposium

Mon-PS2-001

Contribution of psychological factors to the affective reactions towards food taste in under- and over-nutrition

David Garcia-Burgos

Department of Psychobiology, Institute of Neurosciences, Biomedical Research Centre, University of Granada. Avda. del Conocimiento s/n, 18100 - Armilla, Granada, Spain.

[Invitation pre-symposium ECRO 2021] The experience of eating and drinking is a complex and multifaceted process in which taste perception plays an important role. In particular, taste perception has been implicated in the modulation of ingestive behaviour such as food preferences and intake patterns. Importantly, previous work on this subject is largely based on the idea that individuals with impaired taste perception may have altered eating behaviours that contribute to diet- and nutrition-related conditions including malnutrition or obesity. To further characterize the relationship between taste perception and weight status, we carried out the sensory and affective analysis of responsiveness to sweet and bitter tastes in healthy subjects, patients suffering from eating disorders and individuals with different weight categories (underweight and overweight). Using multiple-sip temporal-liking, time-intensity and signal detection methodologies as well as automatic facial expression analysis, we found that the affective rather than the sensory component appears to be playing a crucial role in the reaction to food items, which may be biased and exacerbated by motivational states such as hunger or stress. Our results also suggest that variations in the ability to discriminate between sweet-fat mixtures among weight status categories are redundant to the extent that such differences are no clinical significance in actual intake behaviour. Funded by the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement Nº 754446 – Athenea3i.

Mon-PS2-002

New perspective on taste perception: the possible contribution of oral microbiota

Camilla Cattaneo, Ella Pagliarini

Sensory & Consumer Science Lab (SCSLab), Department of Food, Environmental and NutritionalSciences (DeFENS), University of Milan, Italy

It is well known that food choices and eating habits are mediated by a number of biological and environmental factors. Taste is considered one of the main predictors of individual food selection and varies greatly among individuals. Thus, is important to understand how, and to what extent, individual variability can determinately contribute to explain food preferences and behaviors. Moreover, with increasing prevalence of diseases related to over nutrition, there is considerable interest in identifying the factors that could predispose individuals to such disease by influencing dietary decisions. It has been suggested that also microbes in the gastrointestinal tract could have a potential direct role in shaping eating behaviours and food preferences. This presentation focuses on associations between individual differences in sensory perception, oral microbiota and eating habits among adults and children. Despite this novel topic has not been systematically investigated so far, there are some recently results showing the link among these variables. Results are still fragmented, and the overall picture is under construction. However, both the scientific community

and society needs the expertise of the sensory scientists to solve the multidisciplinary tasks and to provide further insights into the complexities of human eating behaviors.

Mon-PS2-003

Winged brains, bugs, nutrients, and behavior

Carlos Ribeiro

Champalimaud Foundation

A balanced intake of different classes of nutrients is a key determinant of health, wellbeing, and aging. We want to understand how animals decide what to eat and how these decisions affect the physiology of the animal. To achieve a mechanistic, integrated, whole-animal understanding of nutritional decision-making we work at the interface of behavior, metabolism, microbiome, and physiology in the adult *Drosophila melanogaster*. I will discuss how the powerful combination of neurogenetics, automated, quantitative behavioral analyses, nutritional and microbial manipulations, and activity imaging approaches is allowing us to achieve a mechanistic understanding of how neuronal circuits interact with organ systems and the microbiome to implement proto-cognitive behaviors and regulate them according to internal states. Adapting nutrient specific appetites to the needs of the animal allows these to optimize important traits such as aging and reproduction.

Mon-PS2-004

Bitter gourd (*Momordica Charantia* L.) stimulates the secretion of the incretin Glucagon-like peptide-1 by enteroendocrine cells *in vitro*

Francisca P. Noya-Leal [1], Shanna Bastiaan-Net [1], Margriet Roelse [2], Maarten Jongsma [2], Renger Witkamp [3], Jocelijn Meijerink [3], Jurriaan J. Mes [1]

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The Glucagon-like peptide-1 hormone (GLP-1) is a key insulinotropic and glucagonostatic incretin produced by the L enteroendocrine cells (EECs) of the intestines. On the luminal side, EECs express a variety of taste receptors, among them, members of the bitter taste receptor family or

taste receptors type 2 (TAS2Rs). The fruit of the *Momordica charantia* is called bitter gourd (BG) and has a distinctive bitter taste. This edible vegetable, common in tropical regions, is also a folk medicine employed for the management of type-2 Diabetes. Within the last decade, there has been increasing evidence on chemosensory activity of EECs, and how food tastants can affect the secretion of intestinal hormones, presumably, by interacting with sweet, umami, and/or bitter taste receptors. We hypothesized that the hypoglycaemic properties of BG (or a part of it) would be based on the stimulation of GLP-1 secretion by EECs, likely through interaction with TAS2Rs. Here, we studied the GLP-1 secretion by *in vitro* EECs (mouse and human) when exposed to different BG specimens (genotypes and extracts). BG samples significantly induced GLP-1 secretion in mouse STC-1 and in human HuTu-80 EECs. Besides, TAS2R16 responded dose-dependently to BG extracts, suggesting its potential involvement in the interaction between BG and EECs. Based on the two EEC *in vitro* models, the GLP-1 secretion induced by different BG cultivars was correlated with antidiabetic effects as found in an *in vivo* piglet study. The role of GLP-1 secretion in BG's antidiabetic effects and the difference between both cell-based models will be discussed.

Mon-PS2-005

Saliva in nutritional sciences: cause or consequence of eating choices?

Elsa Lamy

Mediterranean Institute for Agriculture, Environment and Development, University of Evora

It is unquestionable that unbalanced food choices are one of the main causes of non-communicable diseases, such as obesity, diabetes, or cardiovascular diseases. It is, therefore, essential to understand what influences food acceptance and preferences. Food sensory perception, in mouth, is one of the factors determining if the individual will eat or reject a particular food. Saliva composition plays an important role in this perception, namely by affecting astringency, basic tastes or even retronasal aroma perception. While the participation of saliva in sensory perception must be considered, it is important to bear in mind that its composition is subject to different sources of variation, ranging from genetic factors (what can explain some of the variations between individuals), metabolism and physiology (e.g. influence of appetite/satiety or other metabolic signals), or even factors such as circadian and circannual rhythms, stress or diet cues. As such, all these sources of saliva composition changes, may be also sources of oral food perception. In this presentation, the role of saliva in nutrition will be addressed through two complementary views: 1) the participation of this fluid in the sensory perception of food and, consequently, in its acceptance; 2) the effect of food stimuli (post- ingestive or sensory) in saliva composition. The discussion will be directed to show how this double relationship saliva x food (conditioning its consumption, and/or

being a reflection of it) has a physiological meaning and how it can constitute an opportunity to shape food perception and to contribute for acceptance of healthy foods.

Tue, 14 Sep -09:15 - 10:00

Keynote/Plenary Lecture - Danielle Reed

Tue-K1-001

Twenty years of taste receptors

Danielle Reed

Monell Chemical Senses Center

Before there were molecular tools available to identify and study taste receptors, scientists predicted that there would be many taste receptors and they would respond to specific taste qualities. These predictions came as early as the 1930s, from the results of human psychophysical studies, which showed that some people were selectively unable to taste certain bitter compounds but had an otherwise ordinary sense of taste. These observations suggested that taste perception arose from several or many receptors, and that one receptor could be dysfunctional in some people, leading to a specific ageusia. Further insight came with the molecular discovery of the bitter and sweet/umami receptor families at the turn of the twenty-first century. The newly sequenced human genome allowed investigators to search for DNA motifs such as transmembrane domains, which were likely to be a feature of a taste receptor. Other molecular biology tools were also essential to these discoveries. Since then, scientists have made advances in understanding which taste receptors respond to particular ligands, and in understanding the regulation of taste receptor mRNA expression in taste and other cell types. Additional discoveries made in the last twenty years include the receptors for salty and sour taste and perhaps for the non-traditional tastes such as calcium and fatty acids. There have been a few surprises, including the pattern of taste receptor evolution. This pattern includes the expansion of the taste receptor families in some species and the loss of taste receptors in others, e.g., cats. One discovery that was not a surprise was the molecular basis for specific ageusias, which arise from segregating pseudogenes, receptors that are nonfunctional in some people but not others. The burgeoning availability of DNA sequences for many species and many people worldwide has opened the frontier to better understand the range of perceptual experience among all animals including humans.

Tue, 14 Sep -10:00 - 10:45

Keynote/Plenary Lecture - Chef José Avillez

Tue-K2-001

Food for thought

José Avillez

Belcanto Restaurant

Portuguese and a chef, José Avillez' main focus is to promote Portuguese gastronomy and to contribute to making Portugal a top gastronomic destination. He's considered a reference in Portuguese gastronomy and has stood out because of his enterprising spirit and drive to go further. His immense curiosity, love for traveling and constant drive to experiment and learn have contributed a great deal to his creativity and evolution, though the great source of inspiration is Portuguese cuisine. He defines himself as a chef who's passionate about cuisine and about his country and who embraces innovation and creativity without ever forgetting tradition, quality, authenticity, and the worth of work. José Avillez grew up near the ocean and a pine forest, in Cascais and this had a profound influence on his work. He studied Business Communication in college, had private study lessons with the key author on traditional Portuguese gastronomy, Maria de Lourdes Modesto, and did many professional internships in several different restaurants in Portugal and abroad, such as El Bulli by Ferran Adrià, who transformed his concept of cuisine. In 2008 he took on the role of executive chef of the emblematic restaurant Tavares, in Lisbon, the place where, in 2009, he'd win his first Michelin star. In 2011 he opened his restaurant. Today he has multiple restaurants in Portugal (Lisbon and Porto) and Dubai, each with a different concept, but all expressing his passion for cuisine. In his talk, José Avillez will talk about the creative process behind the creation of new gastronomic creations and wine-food pairings. He will also discuss how he and this team integrate input from multiple sensory systems and combine it with storytelling to help them create the perfect gastronomic experience.

Tue, 14 Sep -11:15 - 12:00

Keynote/Plenary Lecture - Sandeep Robert Datta

Tue-K3-001

Linking the past to the future in olfaction

Sandeep Robert Datta

Harvard University

Efficient sensory codes convey new information while reducing redundancy. Adaptation helps to build efficient codes by allowing neurons and networks to minimize their responses to background stimuli, and conversely to boost signals from stimuli that are unexpected and therefore informative. Thus, by instantiating the prediction that the world now will be similar to the world a moment ago, adaptation enables sensory systems to filter the past and to selectively convey information about novel cues in the future. While mechanisms supporting rapid (e.g., milliseconds to seconds) adaptation have been well characterized in the olfactory system — and reformat fast, dynamic stimuli such as odor plumes — it is not clear whether or how olfactory neurons adapt at the longer timescales at which animals traverse different natural odor environments. Here we describe a novel mechanism for sensory adaptation that enables different odor environments to imprint themselves upon the olfactory system. This mechanism enables the olfactory system to instantiate expectation, thereby building odor codes that are personalized by each animal's specific and ongoing odor experience.

Tue, 14 Sep -14:00 - 15:45

Symposium 1 - Symposium 1

Tue-S1-001

Reconstruction of the mouse olfactory glomerular map using single-cell technologies

I-Hao Wang [1], Evan Murray [2, 9], Gregory Andrews [3, 9], Elisa Donnard [3, 9], Violeta DuranLaforet [4], Hao-Ching Jiang [1], SungJin Park [1], Daniel Bear [5, 6], Dorothy Schafer [4], Manuel Garber [3], Zhiping Weng [3], Fei Chen [2, 7], Evan Macosko [2, 8], Paul Greer [1]

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Massachusetts Medical School, Worcester, MA, USA, [5] Department of Psychology, Stanford University, Stanford, CA, USA, [6] Tsai Neurosciences Institute, Stanford University, Stanford, CA, USA, [7] Department of Stem Cell and Regenerative Biology, Harvard University, Cambridge, MA, USA, [8] Department of Psychiatry, Massachusetts General Hospital, Boston, MA, USA, [9] These authors contributed equally

The olfactory system's ability to detect and discriminate between the vast array of chemicals present in the environment is critical for an animal to be able to forage food, find mates, and avoid predation. In mice, these chemicals are detected by odorant receptor (OR) proteins that are expressed by olfactory sensory neurons (OSNs). Each OSN expresses only one OR, and all OSNs that express the same OR project their axons to a stereotyped position within the olfactory bulb to form a glomerulus. This organization results in a given odorant triggering a unique, but spatially invariant, pattern of glomerular activation, and it is believed that this organization may be critical for assisting the brain in decoding odor identity. However, a major impediment to understanding the computation that transforms patterns of glomerular activity to the decoding of odor identity, is that the positions of only a handful of glomeruli are known. Here, we use spatial transcriptomics and machine learning to reconstruct a map of the majority of glomerular positions within the mouse olfactory bulb. Using single cell RNA sequencing, we find that each type of OSN expresses a unique transcriptional program—beyond simply the OR that is has chosen—that distinguishes it from all other OSNs. These unique transcriptional programs are highlighted by a subset of axon guidance genes, and together are sufficient to predict where within the olfactory bulb the OSN will form its glomerulus. Intriguingly, the transcriptional program of a given OSN is tightly linked to the properties of the OR that it displays, which results in glomeruli that respond to similar odorants being in close proximity to one another. Together, these results provide a new, mostly complete map of glomerular positioning within the mouse olfactory bulb.

Tue-S1-002

Exploring the spatial coding in olfaction with transcriptomics and machine learning

Mayra Ruiz [1, 2, 3], Eman Abou Moussa [4], Antonio Scialdone [1, 2, 3], Luis Saraiva [4, 5, 6]

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Odors are detected by a specialized set of cells called olfactory sensory neurons (OSNs). There are different subtypes of OSNs, which are identified by the olfactory receptor gene (Olfr) they express and detect specific subsets of odourants. OSN subtypes are organized in stereotypic anatomic locations of the olfactory epithelium called "zones". A comprehensive and quantitative

mapping of the zones, as well as an understanding of their function, is still missing. During this talk, I will present the analysis of a spatial transcriptomic dataset that allowed us to build the first transcriptome-wide tridimensional map of the olfactory mucosa (OM). Topographic maps of genes differentially expressed in space reveal that both Olfrs and non-Olfrs genes are distributed in a continuous and overlapping fashion over five broad zones in the OM. Using machine learning methods, we have quantitatively identified the "zones" and characterized their transcriptional signature. Finally, I will show how the distribution of Olfrs inside the zones suggests they might be optimized to enhance odor discrimination.

Tue-S1-003

Mapping of olfactory bulb by targeted capture of olfactory receptors

Hiroaki Matsunami

Duke University

Spatial transcriptomics enable the mapping of cell-type markers within tissues of interest, although limitations arise when cell-type transcriptional markers are expressed in relatively low abundance. Such an issue exists in mapping olfactory glomeruli, which are the fundamental units of the mammalian olfactory bulb and originate from axons from olfactory sensory neurons expressing the same olfactory receptor. We combine target capture enrichment sequencing to overcome low-abundance target expression with spatial sectioning along the anteroposterior, dorsoventral, and mediolateral axes to map 86% of olfactory receptors and generate a three-dimensional model of glomeruli positions on the murine olfactory bulb. Our dataset identifies a unique relationship between specific olfactory receptor residues and olfactory bulb target positions.

Tue-S1-004

Molecular mapping of olfactory bulb input and output

Alexander Fleischmann [1], Nell Klimpert [1], Sara Zeppilli [1], Andreas Schaefer [2]

[1] Department of Neuroscience and the Robert J. and Nancy D. Carney Institute for Brain Science, Brown University, Providence, RI 02912, USA, [2] The Francis Crick Institute, Sensory Circuits and Neurotechnology Laboratory, London, UK, and the Department of Neuroscience, Physiology & Pharmacology, University College London, UK London, United Kingdom

Determining the spatial organization of odorant receptor gene expression in olfactory bulb glomeruli is critical for understanding the functional organization of the olfactory bulb. However, the identity of only a few glomeruli have been mapped thus far. Here, we use spatial transcriptomics to develop a comprehensive map of glomerular identity and domain structure in the mouse olfactory bulb. We developed experimental protocols for efficient odorant receptor transcript capture on barcoded spatial arrays, and we collected tissue sections from an entire olfactory bulb for RNA sequencing. We will present an initial description of the three dimensional organization of odorant receptor and domain marker gene expression in the olfactory bulb. Finally, we will discuss the diversity of olfactory bulb output neurons, mitral and tufted cells, and the preferential connectivity of molecularly defined mitral and tufted cell subtypes with cortical target areas. Our data provide a rich new resource for understanding the molecular mechanisms of olfactory map assembly and its function in odor processing.

Tue-S1-005

A critical period and a feedback mechanism controls odorant receptor expression in Drosophila

Mattias Alenius

Department of Molecular Biology, Umeå University, Umeå, Sweden

Odorant receptor (OR) expression is monogenic in most species. In mouse, an OR feedback loop generate the monogenic expression. In adult Drosophila OR expression is stereotype and suggested to be predetermined, not requiring feedback regulation. Here, we will present an OR feedback mechanism also in Drosophila that early in life refines OR expression. We will show how dLsd1 and Su(var)3-9 balance heterochromatin formation to direct OR expression similar to mouse. We will show that the expressed OR induces dLsd1 and Su(var)3-9 expression, linking OR level and possibly function to OR expression. OR expression refinement shows a restricted duration, suggesting that a gene regulatory critical period brings olfactory sensory neuron differentiation to an end. Consistent with a change in differentiation, stress during the critical period represses dLsd1 and Su(var)3-9 expression and makes the early permissive OR expression permanent. We will further discuss what such a mechanism can do for OR evolution and how the induced permissive gene regulatory state makes OR expression resilient to stress. We will also discuss how the Drosophila critical period fit with mouse OSN differentiation and that the early steps in monogenic OR expression regulation is not so different across phyla.

Tue, 14 Sep -14:00 - 15:45

Symposium 2 - Symposium 2

Tue-S2-001

Unravelling taste perception in honeybees using CRISPR/Cas9

Laura Degirmenci, Ricarda Scheiner

Universität Würzburg Biozentrum, Zoologie II Am Hubland 97074 Würzburg

Honeybees (*Apis mellifera*) depend on floral nectar for carbohydrates and on a diversity of floral pollen as sources of proteins. It is remarkable that they only possess ten gustatory receptors (Grs) for carefully evaluating the diverse floral resources they encounter. The fruit fly, for example, has a broad set of 69 genes for taste perception and the mosquito even has 75 genes. So far, three honeybee taste receptors have been characterized in a Xenopus cell system. For the first time we characterized honeybee taste receptors *in vivo* in adult honeybees employing the novel CRISPR/Cas9 technique. Knocking out individual taste receptors we can show that *AmGr1* double mutants showed a reduced response to sucrose and glucose, but not fructose. *AmGr3* mutants are insensitive to fructose, but not sucrose, confirming that this receptor is a specialised fructose receptor. *AmGr2* mutants did not show any differences compared to wild type bees, confirming that this receptor is a co-receptor only. Our results demonstrate that CRISPR/Cas9 is a strong molecular tool for honeybee research, allowing functional analysis of receptors in live bees combined with behavioural studies.

Tue-S2-002

Neuronal principles underlying internal state dependent decision-making revealed by pan-neuronal volumetric imaging

Daniel Münch, Dennis Goldschmidt, Carlos Ribeiro

Champalimaud Centre for the Unknown, Lisbon, Portugal

When deciding what to eat, animals evaluate sensory information about food quality alongside multiple ongoing internal states. How internal states interact to alter sensorimotor processing and shape decisions such as food choice remains poorly understood. Here, we use pan-neuronal volumetric activity imaging in the *Drosophila* brain to investigate the neuronal basis of internal state dependent nutrient appetites. We created a functional atlas of the ventral fly brain and find that metabolic state shapes sensorimotor processing across large sections of the neuropil. Reproductive state, in contrast, acts locally to define how sensory information is translated into feeding motor output. Thereby, these two states synergistically modulate protein-specific food intake and thus food choice. Finally, using a novel computational strategy, we identify driver lines innervating state-modulated regions and show that the newly identified borboleta region is sufficient to direct food choice towards protein-rich food. We therefore identify a generalizable principle by which distinct internal states are integrated to shape decision-making and propose a strategy to uncover and functionally validate how internal states shape behavior.

Tue-S2-003

Towards better understanding of sweet-tasting molecules

Yaron Ben Shoshan-Galeczki, Masha Niv

1The Institute of Biochemistry, Food Science and Nutrition, Robert H. Smith Faculty of Agriculture, Food and Environment, The Hebrew University of Jerusalem, P.O. Box 12, Rehovot 76100, and Fritz Haber Center for Molecular Dynamics, The Hebrew University,

Sweet taste is mediated via the Family C GPCRs dimer T1R2/T1R3. Most known sugars and sweeteners bind to the Venus Fly Trap extracellular domain of the T1R2 subunit. A possible approach for finding new sweet molecules is through structure-based virtual screening by docking to sugar-binding site. Since no experimental structure of human sweet taste receptors is available yet, we evaluated several homology models and docking protocols by their ability to differentiate between true positives and decoys. The best performing models were then used for prospective virtual screening, uncovering newly patented sweeteners. Next, the model was used for rationalizing structure-activity relationship of compounds derived from licorice, and to discriminate sweet from non-sweet licorice compounds. Non-sweet licorice-tasting compounds did not surpass the docking score of the known sweet compounds. Analysis of docked sweet saponins indicated that it is important to form hydrogen bonds with residues N44 or Y103. The saccharide moiety and the functional group at position C-30 were common among the sweet licorice compounds. The C-30 functional group formed hydrogen bonds with N44. While non-sweet compounds, had lower docking scores, and were oriented towards the lower lobe of the binding site. Finally, though typically a change in chirality strongly affects ligand–receptor interactions, we show that L- and D-

glucose across a few concentrations are perceived as similarly sweet by humans, and that in cell-based functional assays, both enantiomers activate the human sweet taste receptor TAS1R2/TAS1R3. Docking suggested that glucose enantiomers can bind in either one of two subpockets of the VFT domain of TAS1R2, each overlapping with the predicted positions of monosaccharide units of sucrose. The compatability of each of the hydroxyl-rich enantiomer is enabled by multiple hydrogen-bond donors and acceptors in the binding subpockets.

Tue-S2-004

Gamification of sensory testing for humans

Kyle Palmer

Opertech Bio, Inc.

Variability evident in human studies of taste is recognized as a substantial obstacle to a precise understanding of the relationship between tastant receptor activity and resulting taste response. There are many potential sources of variability given that experimental control over human subject-dependent variables is limited. However, one controllable variable in human studies that largely has been overlooked is incentive structure in the experimental design. Generally, subjects are remunerated for their participation in a taste study, but no consequences are associated with their responses during a test. We have developed a technology and associated methodology by which subject performance in taste testing is incentivized through gamification. The approach is based on operant taste discrimination, where consequences are directly and immediately tied to a subject's response on each trial. Under these conditions, responses that accurately identify standard control stimuli are rewarded, and errors penalized, on a trial-by-trial basis. Subjects accumulate a score translated to a monetary value as the session progresses automatically through 96 trials, and the final amount at the session's end is immediately deposited to a PayPal account. By this approach, subjects attain a high degree of taste acuity that is consistently recorded across tests with low variability. Rapid throughput automation of the technology permits collection of large datasets from each subject, further reducing variability. Results from extensive testing using this technology will be presented, reflecting a close correspondence with pharmacological predictions of underlying receptor activity.

Tue, 14 Sep -16:15 - 17:00

Keynote/Plenary Lecture - Linda Buck

Tue-K4-001

Thirty years of olfactory receptors

Linda Buck

Fred Hutchinson Cancer Research Center

The seminal discovery of the odorant receptors by Linda Buck and Richard Axel in 1991 revolutionized the field of chemosensation. In this presentation, Linda Buck will give a brief historical description of the key findings and early challenges around the molecular basis of olfaction, and discuss how recent advances in olfactory neurobiology fundamentally inform our understanding of the interactions between odorants, their receptors in the nose, and emotion.

Tue, 14 Sep -17:00 - 18:00

Posters - Poster Session

Tue-Posters-001

Genetic variation in UGT2A1 is not associated with ratings of odor intensity or pleasantness in human twins

Liang-Dar Hwang [1, 2], Mackenzie Hannum [3], Paule Joseph [4, 5], Alissa Nolden [6], Katherine Bell [3], Cailu Lin [3], Scott Gordon [2], Nicholas Martin [2], Margaret Wright [7], Sarah Marks [3], Akane Kikuchi [3], Aurora Toskala [3], Danielle Reed [3]

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We followed up on a recent report and an accompanying blog post that a particular genotype is associated with more significant smell loss in people with COVID-19 and a worse overall sense of smell in people who are not sick. This genotype is within two genes, the code for enzymes that metabolize odorants like eugenol (but not other odorants like amyl acetate; UGT2A1/A2, UDP-glucuronosyltransferases). A convenience sample of human twins (studied before COVID-19 pandemic) rated six odorants (using scratch and sniff methods) for intensity and pleasantness. We grouped twins by genotype and found no differences in ratings of odorant intensity or pleasantness among those with high vs. low-risk alleles (rs7688383; N=879; all p-values >0.05). Participants with

the high-risk allele rated eugenol intensity (p=0.46) and pleasantness (p=0.83) similarly to people with the low-risk allele. In a small, separate study of 27 twins who had COVID-19, we found that the risk allele did not predict smell loss (p=0.29). We need to test more people with more sensitive psychophysical methods to understand whether this genetic variation affects the sense of smell in people without COVID-19, and this data collection is ongoing.

Tue-Posters-002

Sophorolipid Reduces Bitter Taste in Humans In Vivo and In Vitro

M. Hakan Ozdener, Paul Wise

Monell Chemical Senses Center

Bitter taste warns us against ingesting toxic chemicals but can also discourage the consumption of healthful nutrients and prescribed medications. Thus, the discovery of ingredients to reduce bitterness is an important research priority. The potential bitter-taste-blocking effect of sophorolipids has recently been reported. Sophorolipids are biosurfactant glycolipids normally synthesized via yeast fermentation. In the current experiments, the effect of sophorolipid on bitter taste was evaluated using both cultured human taste papillae (HBO) cells and in vivo sensory experiments with human tasters. Sophorolipids significantly reduced responses of HBO cells to a mixture of diverse bitter compounds. Human participants rated the bitterness of a mixture of diverse bitter compounds as less intensely bitter both after prerinsing with a sophorolipid solution and when sophorolipids were added to the mixture. Taken together, these results suggest that sophorolipids may reduce perceived bitterness in humans, at least in part by acting on peripheral mechanisms. Although further work is needed to confirm these findings and determine the exact mechanism(s) of action, thus far sophorolipids show promise as candidate ingredients to reduce bitterness.

Tue-Posters-003

Odor prediction via graph neural networks and representation learning

Matej Hladiš, Sébastien Fiorucci, Jérôme Golebiowski, Jérémie Topin

Institute of Chemistry, Université Côte d'Azur

Our sense of smell relies on the use of approximatively 400 genes expressing functional odorant receptors (ORs), endowing us with the power to perceive complex chemical space surrounding us. ORs are transmembrane proteins which belong to the family of class A G protein-coupled receptors

(GPCR). Establishing a relationship between the structure of a molecule and the smell it triggers is a long-standing challenge. The first step to crack the combinatorial code of olfaction relies on identification of OR-ligand pairs. Nowadays, the data linking a molecule to a set of ORs remain scarce and only 131 ORs have an identified ligand. Thus, building a machine learning protocol taking ORs' sequence explicitly remains challenging. To tackle this issue, we leverage recent advances in representation learning and combine them with graph neural network (GNN) to build a receptor-ligand interaction prediction model. Several methods inspired by success of representation learning in the natural language processing (NLP) have been proposed to represent protein sequences. Here we use architecture based on BERT model to represent ORs which was previously trained on more than 200M protein sequences. We use the output of BERT as a starting point for receptor representation. We treat ligands as graphs and process ORs and ligands simultaneously using GNN. This receptor-ligand model has been evaluated on a set of more than 7500 OR-ligand pairs. The model is achieving a Matthews correlation coefficient (MCC) of 0.40 in the case that all receptors are included in the training set (i.e. random split). The performance on a much more difficult deorphanization task (i.e. discarding all pairs of a given receptor) remains acceptable with a value of 0.27. As a comparison, an exhaustive in vitro search would lead to a success rate of ~3% and MCC equal to 0

Tue-Posters-004

Exploring the olfactory-cognitive processes that influence odor identification results

Rohan Raj [1], Pawel Herman [2], Jonas Olofsson [1]

[1] Gösta Ekman Laboratory, Department of Psychology, Stockholm University, Sweden., [2] Lansner Laboratory, Department of Computational Science and Technology, Royal Institute of Technology, Sweden

Odor identification (OID) is the most common test of human olfaction; test trials typically involve matching a target odor to a correct label among three distractors. However, the underlying processes are poorly understood. Here, we investigated the OID response patterns in a large population-based sample (n=2479) of cognitively intact older adults (aged 60-100 years) from the The Swedish National Study on Aging and Care in Kungsholmen (SNAC-K) where olfaction was assessed by a 'Sniffin´ Sticks' OID test with 16 odors. First, we analyzed the pattern of mistakes, and the results show that some distractors are much more commonly selected than others. This suggests that cognitive factors may be present. Second, we conducted an online survey of 1000 older adults, aged 60-90 years, who were asked to imagine and rate the olfactory similarity of the target odors and the three corresponding distractors (e.g. "How similar do apple and mint smell?"). Results show that the imagined similarity of the target-distractor pair could partly predict how often

the distractor was mistakenly selected in the SNAC-K experiment. Third, we used data from the Swedish web corpus and Word2Vec neural network algorithm to quantify the semantic association strength between labels of each target odor and its distractors. The semantic distances between target-distractor pairs were found to partly explain the pattern of incorrect responses in the SNAC-K OID test. In sum, our results suggest that OID tests are not just perceptual olfactory assessments, but reflect olfactory cognition and language. Behavioral outcomes are likely influenced by imagining the olfactory qualities corresponding to each odor label and by selecting strongly semantically associated labels. These insights may be harnessed to develop OID tests that are tailored for clinical purposes, for example in predicting the onset of neurological disorders. This research was supported by the Swedish e-science Research Center to PH and JKO.

Tue-Posters-005

Intra-specific individuality of odor-evoked behavior and activity

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Animal behavior, anatomy and physiology can vary significantly among genetically identical individuals. The majority of behavioral studies were conducted at a group level, and only the mean behavior of all individuals was considered.Similarly, in neuronal studies, data were pooled and normalized from several individuals. Nevertheless, individuality is an important aspect of behavior that should not be ignored. Recent studies have shown that behavioural biases and preferences can vary significantly among individuals of the same genotype. Here, we show that a highly inbred Drosophila laboratory strain (CS) stimulated with either aversive or attractive odors exhibit idiosyncratic odor preferences that persist across tests and days. Furthermore, we are currently investigating whether individual odor preferences are reflected by distinct odor response patterns in the fly brain to elucidate the neuronal mechanisms underlying individual odor-guided decisions.

Tue-Posters-006

Visual and auditory processing in human olfactory cortex

Evelina Thunell [1, 2, 3], Behzad Iravani [1], Moa Peter [1], Danja Porada [1], Katharina Prenner [1], Johan N. Lundström [1, 4, 5, 6]

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The piriform cortex, considered part of the primary olfactory cortex, has been found to respond also to stimuli in other modalities in certain conditions. Here, we use fMRI (n = 47) to show that even in the absence of any reference to odors during the experiment, the posterior piriform cortex (PPC) is activated by both pictures and sounds of objects. We also found significant activation by sounds, but not pictures, in the anterior piriform cortex (APC). These activations were elicited both by objects receiving low and high odor association ratings in a post-experiment rating task. In visual and auditory brain regions, we found cross-activations: Pictures activated higher-level auditory cortex and elicited a decreased BOLD signal in primary auditory cortex (A1), and sounds activated primary visual cortex (V1) and elicited a decreased signal in the higher-level visual area LOC. These findings further question the notion of PPC and APC as purely olfactory regions, and in general contributes to a more nuanced picture of modality specificity in olfactory, auditory, and visual cortices. This work was supported by a grant from the Knut and Alice Wallenberg Foundation awarded to JNL (KAW 2018.0152).

Tue-Posters-007

Mapping olfactory system using probabilistic tractography

Divesh Thaploo [1], Akshita Joshi [1], Charalampos Georgiopoulos [1, 2], Thomas Hummel [1]

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To examine association between olfactory function and white matter fibre tracts, using probabilistic tractography, between primary and secondary olfactory areas, i.e. piriform cortex (PIR), orbitofrontal cortex (OFC) and thalamus (THAL). 38 healthy subjects took part in the MRI study and perceived 2 trigeminal odors (peppermint, spearmint) and 2 olfactory odors (strawberry, cherry). Odors were rated for intensity and pleasantness using visual analogue scales. We acquired diffusion tensor images (DTI) on a 3T MR scanner. Image analysis carried out using FMRIB software library. We performed tracking with PIR as the seed mask. Connections between PIR and OFC were termed as direct and between PIR and THAL as indirect. A Kruskal-Wallis test revealed a significant difference based on the type of the track. Higher number of tracks, for the olfactory system, were found on the right side of the brain as compared to the left side (p=0.001). Also, higher

number of indirect tracks were found on left side (p=0.004) and on right side of the brain (p=0.01). A partial correlation analysis (age as control) revealed a positive correlation between direct tracks (PIR to OFC) on left side and threshold score for trigeminal odors (r=0.40, p=0.01). Left and right indirect track path (PIR to THAL) had a positive correlation with intensity ratings for trigeminal odors (r=0.40, p=0.01 and r=0.33, p=0.03, respectively). We also found a positive correlation between right indirect track path and odor identification score (r=0.37, p=0.02). Overall, we found higher tracks for the right hemisphere of the olfactory cortex. Higher number of direct tracks correlated with higher odor threshold scores whereas higher number of indirect tracks correlated with higher odor identification scores and higher odor intensity ratings. Importantly, results were derived using a more data driven approach rather than a-priori approach. Study funded by Takasago, Paris, France.

Tue-Posters-008

Indole induced signal transduction pathway in cultured human taste (HBO) cells

M. Hakan Ozdener

Monell Chemical Senses Center

Odorant receptors (ORs) detect volatile molecules and are naturally expressed in the membranes of olfactory epithelial cells. However, recent studies have shown that odorant (olfactory) receptors are also expressed throughout the body in different tissues, including the kidney, brain, sperm cells, skin, prostate, and gut. We recently demonstrated the functional expression of human ORs in cultured human fungiform taste (HBO) cells. In this study, we aimed to explore the signal transduction pathway activated by the odor, indole, in HBO cells. Indole has a flowery odor at low concentrations and a fecal odor at higher concentrations. Using single-cell calcium imaging, indole induced transient intracellular calcium signals in HBO cells by activating an adenylyl cyclase signaling pathway. In addition to the canonical olfactory signaling pathways, several transient receptor potential cation channels (TRPs) such as TRPA1 and TRPV1 were also implicated in indole-induced responses. These results confirm the presence of similar odor-mediated signal transduction pathways in both human taste cells and olfactory cells. In addition, these data suggest that HBO cells can be used to screen a variety of odorants against chemosensory receptors. This platform provides a mechanistic approach for identifying receptor agonists and antagonists that can be used to produce novel odors eliminate malodors.

Tue-Posters-009

Long-term exposure with sucrose regulates gene expression of nutrient-sensing pathways in human intestinal cell models

Verena Preinfalk [1, 5], Sarah Stadlmayr [1, 5], Jakob P. Ley [2], Veronika Somoza [3, 4], Barbara Lieder [1, 3]

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One way to reduce the energy content of foods while maintaining the sweet taste is the application of non-caloric sweeteners. However, knowledge regarding the consequences of a long-term exposure to sweeteners on gene expression of sweet sensing pathways in the human intestine is scarce. Here we investigated the impact of three common non-caloric sweeteners in comparison to sucrose in equi-sweet and equi-molar physiologically relevant concentrations on gene expression of nutrient-sensors in cell culture models of the small intestine. A coculture model of Caco-2 enterocytes and mucus-producing HT29-MTX-E12 goblet cells in comparison to Caco-2 cells in monoculture was established to obtain a physiologically more relevant model. Both cell models were treated during differentiation with either sucrose, rebaudioside M, sucralose, or neohesperidin dihydrochalcone for 7, 14, or 21 days, and the gene expression of *TAS1R3*, *SLC2A2*, *SLC5A1* and *KCNJ8* was analyzed by qRT-PCR. The coculture model showed a physiologically more relevant transepithelial electrical resistance and mucus production than the monoculture, in addition to an in vivo-like paracellular permeability. Treatment with the sweeteners led to less pronounced regulation of the target gene expression in the coculture model. The treatment with sucrose applied in an equi-sweet concentration to the non-caloric sweeteners had the strongest impact on the expression of the target genes, e.g. a 1.44 ± 0.05 -fold ($p < 0.0001$) increase in *SLC5A1* expression was detected after 14 days of treatment with sucrose, but not the other sweeteners in Caco-2 cells. The results further indicate that there was no impact of the sweet intensity on the expression of the marker genes. In conclusion, structure-specific effects for sweeteners on gene expression of nutrient sensing pathways were demonstrated in the cell models for the human intestine, with stronger effects in the Caco-2 monoculture than in the coculture model using goblet cells.

Tue-Posters-010

Integration of olfactory and visual objects with verbal cues: An fMRI study.

Stephen Pierzchajlo [1], Teodor Jernsäther [1], Lara Fontana [3], Massimiliano Zampini [3], Jonas Olofsson [1, 2]

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Humans are often bad at identifying odors, but extremely skilled at identifying visual objects. A possible explanation is that olfaction may rely to a high degree on other senses to enhance identification, given the olfactory cortex's direct association with integrative brain nodes. This idea was recently supported by a behavioural study in which we asked participants to match visual and olfactory target stimuli to preceding verbal cues that were either congruent or incongruent with the predicted targets' identity. Olfactory target matching was more affected than visual matching by the cue-target congruency. Several studies have provided evidence that the piriform cortex (PC) is the key olfactory area responsible for generating predictive models of olfactory stimuli. Under the predictive coding framework, stimulus processing is generated not by expected stimuli, but by error signals responding to expectation violation. If olfactory identification is indeed more reliant on other senses than vision is, the PC and visual cortex (VC) should be differentially affected by expectation violations, and the subsequent patterns of neural activation should diverge more in the PC. Empirical results of an ongoing fMRI study testing this hypothesis will be presented at the ECRO meeting. In line with predictive coding research in vision, our preliminary data (n=15) show that the piriform cortex is more activated to incongruent olfactory stimuli. Additionally, we expect congruency to affect neural pattern decoding of olfactory targets more than visual targets. Finally, we expect the representational content of congruent stimuli to be more different from incongruent stimuli in the PC compared to the VC. This approach will yield new insights into how identities may be differentially represented in the sensory cortices of the brain. The research was supported by the Swedish Research Council (2020:00266) and Knut and Alice Wallenberg Foundation (2016:0229) to J.K.O.

Tue-Posters-011

Chemical senses can serve the UNESCO Cultural Heritage of Humanity: the case of the red palm weevil pheromone receptor

Binu Antony [1], Nicolas Montagné [2], Rémi Capoduro [2], Arthur Comte [2], Krishna Persaud [3], Corrado Di Natale [4], Arnab Pain [5], Emmanuelle Jacquin-Joly [2]

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The date palm has been connected to the population of many countries for centuries, serving both as a key food source, crafts, professions, social and cultural traditions. Because of that, date palm-related knowledge, skills, tradition, and practices were inscribed in 2019 on the representative list of UNESCO's intangible cultural heritage of Humanity. However, palm tree cultivation is threatened by the global expansion of an invasive, quarantine insect pest that infests these trees; the red palm weevil (RPW), *Rhynchophorus ferrugineus*, it's number one enemy. The success of this species results in part in its efficient chemical ecology, and in particular, its pheromonal communication. This species uses an aggregation pheromone produced by males and that attracts both males and females for feeding and mating, resulting in a mass attack of the trees. A better understanding of the molecular mechanisms of pheromone detection may help optimizing trapping solutions and identifying new targets for this pest control. In this context, we report here the identification and functional characterization of the first RPW pheromone receptor by a combination of omics, loss-of-function, and heterologous expression approaches. The identification of this pheromone receptor opens up new perspectives for the RPW control. First, it appears to be a promising target for the design of receptor agonists/antagonists/blockers, disturbing the weevil pheromone detection and the associated behavior. Second, as this receptor represents an excellent RPW pheromone detector, it will be used to develop a new generation of bioinspired sensors based on natural protein detectors. Such sensors will allow early detection of the pest, a pivotal step to prevent invasion.

Tue-Posters-012

Comparison of two sensory methods to obtain reliable dose-intensity curves for sweet taste compounds

Noëlle Béno, Gaïa Maillard, Thierry Thomas-Danguin

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This study aimed to compare two methods for delivering sweet solutions that were evaluated for sweetness intensity by a panel of 26 trained subjects: a Classical Sensory Analysis (CSA) and a Gustometer-assisted Sensory Analysis (GSA) method. CSA was based on 10 mL samples delivered monadically, in plastic cups, to the subjects placed in separate booths. The GSA was based on a Burghart Multistimulator delivering pulses of 400 µl liquid samples in the mouth of one at time participant. Three kinds of sweeteners were used: a bulk sweetener (Sucrose), an intensive natural sweetener (Rebaudioside A), and an intensive artificial sweetener (Cyclamate de Sodium).

The three compounds were diluted in Evian® water at various concentrations. A total of 6 concentrations levels were evaluated by each subject for each sweetener. The subjects were extensively trained for each method to evaluate sweet taste intensity on an anchored linear scale having 6 intensity reference levels corresponding to 6 sucrose-in-water concentrations. Dose-response curves were modeled for each sweetener and each subject, and also at the panel level. Both methods were compared based on individual and panel half-maximal effective concentrations (EC50) values and dispersion. In the end, the whole data collection took almost the same time for the two methods. Whereas CSA was more comfortable for subjects and allowed to test up to 16 subjects in a single session, GSA allowed to test more samples and to include replicates, which increased results precision. Moreover, GSA required less sample preparation since the gustometer used only a stock solution to perform dilutions automatically, and produced less amount of waste (plastic cups). In conclusion, GSA is a precise method, easy to use for the experimenter, ecologically relevant, and correctly reflects CSA's more usual tasting conditions.

Tue-Posters-013

Development of an *in vitro* model of oral mucosa to investigate a new hypothesis on the molecular origin of astringency.

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Centre des Sciences du Goût et de l'Alimentation, UMR1324 INRAE, UMR6265 CNRS Université de Bourgogne, Agrosup Dijon, F-21000 Dijon, France

Astringency is described as an oral tactile perception occurring during the consumption of tannin-rich foods. This sensation, mediated by the trigeminal nerves, participates negatively to the flavor of foods leading to the rejection of food with high astringency by the consumer. The exact molecular mechanism of its origin and the nature of the sensory receptors activated are still under debate. Up to recently, the main hypotheses involved changes in the lubrication properties of the oral cavity triggering the activation of mechanoreceptors. Recently, we have put a new hypothesis involving the mucin MUC1 forward as an explanation of the origin of astringency. MUC1 is a transmembrane mucin with two subunits linked by non-covalent interactions. It is expressed at the surface of oral epithelial cells impacting on the surface lubrication and the anchoring of the salivary proteins composing the mucosal pellicle (MP). MUC1 is also described as a sensor of the external cellular medium. Thus, we have proposed that MUC1 aggregation by astringent compounds disrupts its two subunits, inducing two different and sequential mechanisms: an intracellular signalling pathway leading to the release of neurotransmitter activating trigeminal free ending nerves and a disruption of the MP increasing the friction forces at the surface of the mucosa. To investigate this hypothesis,

we have developed an innovating in vitro model of oral mucosa based on the transfection of the TR146 oral epithelial cell line with genes coding for different isoforms of MUC1, which differ by the length of the variable number of tandem repeat (VNTR) module and the cleavage of proprotein at the origin of the 2 subunits. Stable expression clones have been selected and their ability to anchor salivary proteins and form the mucosal pellicle has been compared to the one of a previous TR146 cell line transfected with a non-cleavable isoform of MUC1 that do not have a VNTR module.

Tue-Posters-014

Association between well-being and odor perception

Akshita Joshi [1], Vanda Faria [1, 2, 3], Henriette Hornstein [1], Jonathan Warr [4], Thomas Hummel [1]

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We aimed to investigate (1) the neural processing underlying olfactory perception in people with distinct 'levels' of well-being [WB] and (2) the central-nervous processing of odors associated to various degrees with WB. The experiment was comprised of two sessions: Pre-testing and functional magnetic resonance imaging (FMRI). During pre-testing 100 subjects rated intensity, valence and WB associated with 14 generally pleasant odors. From this, we selected two odors (flower+ orange) strongly and two odors (grass+ coffee) weakly associated to WB which were delivered to 43 subjects during 3T fMRI. In presence of odors strongly and weakly associated with WB, the low WB group had strong activation for contrast ON > OFF in bilateral angular gyrus, left inferior frontal gyrus for former odor group and posterior orbitofrontal cortex extended to insula, bilateral inferior frontal gyrus for the latter. However, the high WB group showed major activation in left lateral orbitofrontal gyrus only in presence of odors strongly associated to WB. When comparing high and low WB group, low WB group showed stronger activation than high WB group in the right angular gyrus when perceiving strongly associated WB odors whereas no voxel survived analyses for weakly associated WB odors. Odors strongly related to WB produced a higher activation in subjects with low WB compared to subjects with high WB. This was possibly due to the low WB group being more sensitive to odors that added an emotional value and meaning to them. To conclude, odors and WB state mutually influence each other. This study was supported by Takasago Inc., Paris, France.

Tue-Posters-015

Joint subjective cognitive and olfactory complaints: A population-based, descriptive study

Nira Cedres [1, 2], **Andrea Aejmelaeus-Lindström** [1], **Ingrid Ekstrom** [3], **Jonas K. Olofsson** [1]

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Subjective cognitive decline (SCD) and subjective olfactory decline (SOD) are frequently reported in the elderly population. SCD and SOD may both predict cognitive decline and dementia onset. However, it is unclear to what extent these complaints co-occur in the general population. If the overlap is high, then SOD might just be a reflection of general cognitive complaints, and SOD could be disregarded. We aimed to describe the occurrence of SOD, SCD and their overlap in individuals from the general population. We used data from a population-based sample in Sweden, aged 35 to 90 years (n=803; 50.9% female). The sample was split into healthy controls, SOD, SCD, and individuals reporting both SOD and SCD. SCD was operationalized based on a single question referring to memory ability. SOD was operationalized based on a single question referring to olfactory ability. We used independent samples t-test to compare the SCD and SOD groups regarding age, sex, education, olfaction and cognitive performance. SOD were present in 21.1% whereas SCD were present in 9.9% of participants. Only 2.7% of participants reported both SOD and SCD. Only 12.9% of SOD reported SCD, whereas 27.5% of those with SCD reported SOD. SOD individuals were significantly older and showed poorer olfactory performance compared to SCD. There were no differences between SCD and SOD regarding sex, education and general cognitive status. SOD often occur independently of SCD in the population, suggesting that they are generally independent risk factors. However, among SCD individuals SOD is relatively common, suggesting that cognitive complaints may involve olfaction. The biological causes underlying SOD and SCD, as well as their risk for future cognitive impairment, needs further investigation. The research was supported by the Swedish Research Council (2020:00266) to J.K.O.

Tue-Posters-016

Differences in mouthfeel specified as the changes in salivary flow and viscoelasticity after orosensory stimulation with sucrose and non-caloric sweeteners.

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Taste impressions are not only based on the activation of taste receptors, but also trigeminal stimuli and tactile impressions, also known as mouthfeel. Among others, the mouthfeel is thought to depend on several characteristics of saliva, which are known to be influenced by tastants. However, the impact of sweeteners on saliva characteristics is not well understood. Here, we investigated the impact of selected sweet tasting compounds on the salivary flow and its viscoelastic properties including the oral microbiome in a randomized, cross-over human intervention study with 21 healthy subjects. The flow rate and viscoelasticity of saliva as well as potentially influencing factors thereof were analysed before orosensory stimulation with sucrose, rebaudioside M (RebM), sucralose, neohesperidin dihydrochalcone (NHDC), and water as volume-control, as well as in the first and the second minute afterwards. The results show that all test solutions enhanced the salivary flow after the first minute, with Reb M showing the strongest stimulating effects compared to water (+0.41 g/min, $p < 0.05$). The individually perceived sweetness correlated moderately with the increase in flow rate ($r = 0.3$, $p < 0.01$). The viscoelasticity of saliva was not altered by the test compounds but was associated with the mucin 5B concentration ($p < 0.05$), and an interaction of the test compounds with sweet threshold, and basal elasticity (ANCOVA, $p < 0.05$). Moreover, the elasticity and phase angle of the saliva samples differed between subjects with high or low sweet sensitivity ($p < 0.05$) after stimulation with sucrose. The composition of the oral microbiome was neither associated with the changes in the salivary characteristics, nor with the individual taste perception. In conclusion, this study indicates an impact of predominately cognitive sweetness perception on salivation, and that the complex viscosity after stimulation with sucrose differs between high and low sweet taste sensitive test persons.

Tue-Posters-017

Reverse chemical ecology leads to the identification of new agonists of insect odorant receptors

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Odorant receptors (ORs) are transmembrane proteins expressed in animal olfactory sensory neurons. They are at the core of odorant detection since they recognize odorants and trigger a neuronal response that will be transmitted to the central nervous system. However, most of these ORs are still orphans, which means the odorants that activate them are unknown. The so-called "reverse chemical ecology" or "molecular chemical ecology" approaches propose to use OR-ligand and/or OR-sequence characteristics to identify potential new ligands via a combination of modelling and experimentation, which have the potential to accelerate the discovery of new ligands. Using the crop pest moth *Spodoptera littoralis* (Lepidoptera; Noctuidae), we used such approaches for the study of insect ORs. Ligand-based virtual screening coupled to experimental validation led us to extend the range of semiochemicals active at the receptor and the behavioural levels. Our work opens new routes for i) odorant receptor function analysis, ii) a better understanding of this species odor space, and iii) the development of novel insect pest control strategies targeting chemosensory receptors.

Tue-Posters-018

Body odour disgust sensitivity is associated with xenophobia: Evidence from 10 countries during the COVID-19 pandemic

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Body odour disgust sensitivity (BODS) is assumed to be a behavioural pathogen avoidance function that may also involve social attitudes, favoring less inter-group contact. Previous research showed that among individuals living in the USA, high levels of BODS were associated with stronger xenophobic attitudes, as measured by a scenario involving a fictitious group of refugees. To test the generalizability of this finding, we investigated the relationship between BODS and xenophobia in a multi-national sample of 10 countries across 6 continents. The data was collected during

COVID-19 pandemic, a salient global pathogen threat. Data were collected in Sweden and Italy (N = 2474) during the first pandemic wave, and in The United Kingdom, Canada, New Zealand, Nigeria, Kenya, Hong Kong, Chile and Mexico (N = 4368) during the second wave. Using structural equation modeling, we found support for the preregistered hypotheses that BODS was associated with more xenophobic attitudes, and this relationship was in part explained by perceived dissimilarities of the refugees' norms in terms of hygiene and food preparation. Our results indicate that the positive relationship between BODS and xenophobia is robust across cultures. Our results also support the theoretical interpretation that embracing "traditional norms" might constitute a bridge between pathogen avoidance and social attitudes; traditional norms often involve behaviours that limit inter-group contact, social mobility and situations that might lead to exposure to pathogens.
This work has been supported by the Swedish Research Council (2016-02018) to M.T.L.

Tue-Posters-019

Prediction of sweetness potency from sweet taste receptor dose-response curves.

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People pay attention to their diet, especially sugar intake. The food industry faces the challenge to reduce sugar in food and using low-calorie sweeteners that are healthy, sustainable, and also provide the expected sweet taste quality and intensity. This study aimed at characterizing sweeteners' intensity by two different methods: (i) an *in vitro* method based on a cellular assay and (ii) an *in vivo* method based on a psychophysical approach. Sweet taste is mediated by a single heterodimeric TAS1R2/TAS1R3 receptor that recognizes a wide variety of sweet-tasting compounds including natural sugars, synthetic and natural sweeteners. Following the *in vitro* method, the functional activity of the sweet taste receptor was measured for a series of sweeteners by calcium assay after the expression of TAS1R2/TAS1R3 in heterologous HEK293 cells. In the *in vivo* approach, the sweet taste intensity of the same sweeteners was rated by a panel (n=21-28) of highly trained subjects (18-65 y.o.) using a dedicated ratio scale anchored with 6 sucrose solution references. Natural sugars (sucrose, lactose, fructose), alternative sweetener (fructo-oligosaccharides), high-intensity natural (rebaudioside A and M), and synthetic (sodium cyclamate, sucralose, and acesulfame K) sweeteners were tested. For each sweetener, dose-response curves from both *in vitro* and *in vivo* approaches were modeled by non-linear regression using R software. From these curves, the half-maximal effective concentration (EC_{50}) was estimated for both

methods. A regression model was applied to the relationship between *in vitro* EC_{50} and the sweetness potency (SP) of the sweeteners ($r=0.93$, $p<0.001$). A solution of sucrose 3% was selected as a reference for SP since it corresponds to the *in vitro* sucrose EC_{50}. The regression model was validated using external data obtained for brazzein. Therefore, the model can predict SP based on *in vitro* testing and can be used to rapidly screen existing or new sweetener candidates.

Tue-Posters-020

Recording natural olfactory scenes with temperature-modulated MOX sensors

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Animals and insects rely on olfaction to navigate their environments. One way to understand the strategies they employ and the computational bases of this behaviour is the synthetic approach: as the capability gap between biological and artificial olfaction becomes smaller, it becomes possible to explore a greater range of olfactory-driven behaviours with robotic experiments. But experiments with electronic noses are often performed in laboratory conditions. These are not representative of an animal's natural environment, which can be considerably more challenging due to the uncontrolled influences of humidity, temperature and wind. We set out to collect a dataset that would give us more insights into the olfactory landscapes encountered in the field, exploring whether the data from electronic nose recordings can support navigation bio-inspired sensing strategies such as those based on intermittent odour encounters (bouts). For this purpose, we built a mobile electronic nose that can acquire day-long field recordings from multiple channels of metal-oxide gas sensors, together with environmental conditions like humidity, temperature and atmospheric pressure, geolocation, orientation, and acceleration data. Our system can simultaneously record the responses to odorants and modulate the sensor temperature, an active sensing technique which shows promise for improving the temporal resolution and odorant specificity of the gas sensor signal. This lets us explore a variety of heater modulation techniques and how these should be adapted in real-time to varying environmental conditions. We believe it will prove particularly useful in solving open questions in artificial and biological olfaction. Once embedded on a mobile robot it will also allow these strategies to be validated within a closed sensorimotor loop. DD and MS were funded from EU H2020 Grants 785907 and 945539 (Human Brain Project). MS was funded by MRC grant MR/T046759/1 (NeuroNex: From Odor to Action).

Tue-Posters-021

Human fetal reactions to maternal ingestion of flavours conveying bitter taste: A comparison to a control group

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A fetus is exposed through maternal diet to a wide range of flavours in the amniotic fluid containing olfaction, gustation and trigeminal chemesthesis. The influence of prenatal flavour exposure on chemosensory development has been measured in non-human fetuses or inferred postnatally in reactions to flavours by human neonates. Currently, there are no direct investigations of human fetal facial responses to specific flavours transferred into the amniotic fluid through the diet of pregnant women. In this study, we examined whether fetal fine-grained facial movement profiles in response to maternal consumption of kale flavour (n=34) differs compared to a control group (n=30) of fetuses not exposed to the specific flavour. Fetal facial movements at 32 weeks gestational age were recorded with a Voluson G8 ultrasound and coded frame by frame offline using a standardised coding scheme (Fetal Observable Movement System). Results indicated that fetuses exposed to kale flavour displayed significantly more of AU10 (upper lip raiser), AU16 (lower lip depressor), AU20 (lip stretch), and AU24 (lip presser) in comparison to the control group of fetuses at 32 weeks ($p < 0.001$). These results evidence that fetuses have chemosensory abilities and react to kale flavour conveying “bitter” taste prenatally with specific facial movements. Results are discussed in terms of wider implications of prenatal flavour learning.

Tue-Posters-022

Bitter taste receptor TAS2R4 is involved in regulation of mechanisms of gastric acid secretion induced by gallic acid

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Red wine is an admired beverage, considered to be the healthiest among wines as it provides antioxidants from the dark skin of the grapes. Among these are the characteristic phenolic compounds in red wine, which contribute predominantly to the distinctive taste of red wine. Gallic acid (GA) is one of the major phenolic compounds with evidence for its contribution to the astringent sensation whereas this is not clear for the bitter taste. In our previous studies, we showed that bitter compounds act as regulators on the cellular proton secretion (PS) via extra-oral bitter-taste receptors (TAS2Rs). Furthermore, we showed that red wine is stimulating the PS more effective than white wine. This study was performed with the hypothesis that GA plays a contributive role to the red wine-stimulated effect on PS in human gastric tumor (HGT-1) cells. Sensory tastings pointed out that GA [10 µM] tastes significantly more bitter than tap water, whereby the bitterness is increasing with the concentration of GA. In cell culture studies with HGT-1 cells, the lowest GA concentration perceived bitter was 10 µM, which also evoked a bitter receptor-associated response on the PS by HGT-1 cells. For the investigation of the GA-evoked proton secretion in a red wine matrix, HGT-1 cells were exposed to red wine samples spiked with up to 10 µM GA. These results demonstrated distinct effects of two red wines (Zweigelt and Blaufränkisch) on PS by HGT-1 cells to be modulated after spiking with GA up to a concentration of 10 µM GA. Subsequent gene expression analysis of TAS2Rs revealed TAS2R4 as one of the most prominently regulated genes (1.59±0.22, $p \leq 0.05$). The proposed functional involvement of TAS2R4 in the PS was verified via a homozygote CRISPR Cas9 TAS2R4 knock out approach in HGT-1 cells. These results suggest a functional role of TAS2R4 in the GA-evoked PS, a key mechanism of gastric acid secretion. Moreover, these data provide evidence for making red wine variants more stomach friendly.

Tue-Posters-023

Synchronous Infra-Slow Oscillations Organize Ensembles of Accessory Olfactory Bulb Projection Neurons into Distinct Microcircuits *In Vitro* and *In Vivo*

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Controlling social and sexual behaviour, the accessory olfactory system is indispensable for most mammals. The accessory olfactory bulb (AOB) represents the first stage of information processing in the accessory olfactory system. Here, a subpopulation of mitral cells, which represent the sole projection neurons in the AOB, exhibit infra-slow periodic discharge. AOB mitral cells directly innervate regions in the medial amygdala and hypothalamus that control neuroendocrine state and / or behaviour. However, the physiological mechanisms that underlie AOB mitral cell default output remain controversial. In addition, whether rhythmic infra-slow activity patterns exist in awake behaving mice and whether such activity reflects the functional organization of AOB circuitry remains unclear. Here, we show that AOB mitral cell ensembles form synchronized microcircuits, subdividing the AOB into distinct functional clusters. Using a miniature microscope, we recorded Ca^{2+} transients within the apical dendritic compartments of large AOB mitral cell ensembles in vivo. Using Cre-loxP mouse genetics to selectively label AOB mitral cells, we show that infra-slow periodic activity patterns reflect the idle state of AOB output in awake male and female mice. In addition, confocal time-lapse imaging in acute brain slices shows that ensembles of mitral cells cluster into distinct microcircuits that exhibit correlated Ca^{2+} transients. Our results indicate that synchronous oscillatory discharge of AOB mitral cells plays a key role in information processing in the accessory olfactory system, subdividing the AOB into functional microcircuits, each characterized by a distinct default pattern of infra-slow rhythmicity.

Tue-Posters-024

The influence of hexanal, or lack thereof, on trust in human-robot collaboration

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In a world where human-robot collaborations are becoming increasingly important, facilitating trust in robots is essential. In humans, the level of interpersonal trust is partially determined through the sense of smell. Van Nieuwenburg et al. (2019) built on this idea and found that hexanal increases trust in humans. Based on their findings, the present preregistered study aimed to investigate whether hexanal could also increase the level of trust during human-robot collaboration. It was hypothesized that unmasked and eugenol-masked hexanal would increase the level of trust in human-robot interaction, suggesting a subconscious effect of hexanal on trust. These hypotheses were tested using a double-blind within-subjects design. Two experiments (n = 44 and n = 46) with sufficient statistical power to find the effects from Van Nieuwenburg et al. (2019) were conducted, serving as a direct replication of each other. Trust was operationalized using a visual detection task, where the human participant collaborated with a social robot. The participant indicated whether

they had seen a target, after which they had the option to change their answer to the robot's. Trust was operationalized as the number of times participants changed their answer to the robot's. Subjective trust was also measured using the Reliance Intention Scale. These tasks were performed over four odor conditions: hexanal, eugenol-masked hexanal, eugenol, and a neutral control condition. Contrasting previous work, a comparison of the conditions showed no significant effect of unmasked or eugenol-masked hexanal on the level of trust in robots. Effects of the odors on mood and arousal were ruled out. The findings are considered in the context of a potential mismatch between the natural smell of hexanal and the mechanical context of the robot. This raises new questions: would the effect be found in a different setting, with a different smell, or a more human-like robot?

Tue-Posters-025

Response plasticity of *Drosophila* olfactory sensory neurons.

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In olfaction, sensitization refers to the amplification of a weak olfactory signal when the stimulus is repeated within a specific time window. This occurs at the level of olfactory sensory neurons (OSNs) where odorant receptors (ORs) are housed. Out of the ~60 ORs in *Drosophila melanogaster*, sensitization has been observed in only a few types. Therefore, whether the ability to sensitize is a general property of OSNs is still unknown. The mechanism has been partially elucidated, however the regulation of the process in the different neuronal compartments (i.e. soma, inner dendrite, outer dendrite) it is still not clear. In addition, mitochondria could also play a role in OSNs sensitization since they have been shown to shape the olfactory response. In our study we addressed these questions by characterizing sensitization in a set of seven OSNs with different valence and tuning properties. Using a combination of single sensillum recordings (SSR), calcium imaging and pharmacology, we show how the olfactory signal is processed at the periphery, and find that sensitization is not a general property. In our selected OSN population, sensitization is restricted to those with positive valence. Finally, we demonstrate that mitochondria play an active role in sensitization by acting as intracellular Ca^{2+} buffer.

Tue-Posters-026

Neural response to flavor measured during a sip-and-swallow protocol with EEG

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Brain responses to food or flavor stimuli are usually measured with functional magnetic resonance imaging. One advantage of using electro-encephalo gram (EEG) is reduced cost and the ability to include participants with a higher BMI (compared to functional MRI). In addition, because the participant is seated, EEG allows for a more naturalistic eating context. Event- related EEG studies using sip-and-swallow protocols do not exist to our awareness, but this is a critical lack, as the swallow breath contains flavor. Here we present preliminary data from a sip-and-swallow protocol with event-related EEG responses time-locked to swallowing of a food stimulus (chocolate milk). The participant sipped the stimulus on 50 trials upon hearing an auditory cue. EOG electrodes that are normally used for detection of eye movements are connected on the submental muscle under the participants' chin and utilized for detection of swallowing to obtain a precise time point for consumption event, as well as a regressor for excluding swallowing related noise from the EEG signal. We also tracked sip-size with a USB-readable scale. We have completed data collection on 7 participants (3 women, 4 men). The final sample size will be 15 participants. Ongoing data analyses are done with EEGLAB and ERPLAB software on MATLAB. In conclusion, we demonstrate that a sip-and-swallow EEG protocol is possible with limited loss of data due to movement. Funding: 2232 International Fellowship for Outstanding Researchers Program of TÜBİTAK (Project No. 118C299) to MV. Giract European PhD in Flavor Research Awards 2020/2021 first year PhD research to SA.

Tue-Posters-027

The Social Odor Scale (SOS): development and initial validation of a new scale for the assessment of social odor awareness

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The degree of attention individuals pay to olfactory cues (called odor awareness) influences the role of odors in everyday life. Particularly, odors produced by the human body (i.e., social odors)

are able to carry a wide variety of information and to elicit a broad spectrum of emotional reactions, making them essential in interpersonal relationships. Hence, despite the assessment of awareness toward social odors is crucial, a proper tool is still lacking. Here, we designed and initially validated the Social Odor Scale (SOS), a 12-item scale designed to measure the individual differences in awareness towards different social odors. In Study 1, an exploratory factor analysis suggests that the three factors structure was the model that best fit with the Italian version of the scale. The confirmatory factor analysis (CFA) supports a second-order model with one higher-order factor representing social odor awareness in general and three lower-order factors representing familiar, romantic partner, and stranger social odors. The final version of the scale presented a good fit. In Study 2, CFA was performed in the German version of the scale confirming the validity of scale structure. Study 3 and 4 revealed that SOS total score and its subscales were positively correlated with other validated olfactory scales, but not with olfactory abilities. Moreover, SOS was found to reflect the inter-individual variability that characterizes social odor processing: SOS was related to the gender and reproductive state of the participants. Overall, the results indicated that SOS is a valid and reliable instrument to assess awareness toward social odors in everyday life.

Tue-Posters-028

Identifying Candidate Genes Underlying Isolated Congenital Anosmia

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Approximately 1 in 10,000 people are born with isolated congenital anosmia (ICA), defined as loss of the ability to smell in the absence of other symptoms. Despite the importance of olfaction for our quality of life, the underlying mechanism for these cases of ICA remain largely enigmatic, as only two genes have been implicated, to date. In contrast, the genetic basis of other inherited sensory defects is well investigated, with almost 100 genes implicated in congenital deafness and over 200 genes implicated in congenital blindness. We examined how genetic variation associated with disease state in ten families with congenital anosmia, and determined candidate causal genes for this disorder. Our candidate list included genes for which rare variants were present in family members with congenital anosmia, but not unaffected family members, filtered by dominant or recessive inheritance pattern. There were no candidate genes common to all families, indicating that, as expected, ICA is a heterogeneous disorder with multiple genetic causes. We found several genes that have previously been linked to olfactory function, such as PLEK and CACNA1B. To identify which of the candidate genes are most likely to be involved in ICA, we conducted a targeted

search in a cohort of 121 individuals with ICA (singletons). We identified a smaller list of candidate genes that have a disproportionately large number of variants in this singleton population and investigated them as to their potential role in olfaction. Historically, identification of genes related to other sensory disorders has provided a gateway to better understanding of those senses. Given how few genes have been implicated in olfactory disorders, we have the opportunity to uncover a plethora of new avenues through which to better understand basic olfactory function.

Tue-Posters-029

Rapid Smell Test for Youth with and without COVID-19 Positive Lab-Test Results

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Olfactory dysfunction in children is reported to be less prevalent than in adults, in general and specifically in COVID-19. Yet, olfactory testing is not widespread in the developing population and studies directly measuring smell loss in COVID-19 are sparse. Here we test whether the rapid smell test SCENTinel (version 2.0) can be used in a diverse group of youth to screen for olfactory dysfunction, and in particular COVID-19-associated olfactory dysfunction. A preliminary group of 178 youth (8-15 years old, mean±sd: 11.9±1.59, 58% girls, 65% white) completed the SCENTinel 2.0 test. Eighty-one participants (46% of the sample) received a COVID-19 lab test (8-15 years old, mean±sd: 11.9±1.7 years, 59% girls, 58% white), and N=6 (7%) tested positive (10-15 years old, mean±sd: 12.8±1.6 years, 83% White girls, 17% Non-white boys; days since COVID test range: 12-237 days, mean±sd: 110±79 days) and N = 75 (93%) tested negative (8-15 years old, mean±sd: 11.7±1.7, 25% white girls, 15% non-white girls, 31% white boys, 27% non-white boys; days since COVID test range: 0-493 days, mean±sd: 82±84 days). Although the accuracy for all subtests was nominally lower for the COVID+ group as compared to the COVID- group (detection: 17% vs 16%; intensity: 17% vs. 1%, identification: 17% vs. 13%), no comparison reached the significance level (lowest p = 0.34). Data collection is ongoing and a larger number of COVID+ participants is necessary to make robust statistical considerations. We however demonstrate that SCENTinel can be used in youth to assess olfactory function. This work is supported by NIH RADx-rad initiative U01DC019578.

Tue-Posters-030

Deconstructing the mouse olfactory percept through an olfactory ethological atlas

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Odor perception in non-humans is poorly understood. Here, we generated the most comprehensive mouse olfactory ethological atlas to date, consisting of behavioral responses to a diverse panel of 73 odorants, including 12 at multiple concentrations. These data revealed that mouse behavior is incredibly diverse and changes in response to odorant identity and concentration. Using only behavioral responses observed in other mice, we could predict which of two odorants was presented to a held-out mouse 82% of the time. Considering all 73 possible odorants, we could uniquely identify the target odorant from behavior on the first try 20% of the time and 46% within five attempts. Although mouse behavior is difficult to predict from human perception, they share three fundamental properties: first, odor valence parameters explained the highest variance of olfactory perception. Second, physicochemical properties of odorants can be used to predict the olfactory percept. Third, odorant concentration quantitatively and qualitatively impacts olfactory perception. These results increase our understanding of mouse olfactory behavior and how it compares to human odor perception and provide a template for future comparative studies of olfactory percepts among species.

Tue-Posters-031

Maternal odor favors the categorization of faces in younger, but not older, infants

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In humans, the ability to visually categorize faces (i.e., discriminate faces from other objects and generalize this discrimination across individual faces) follows a protracted development during the first year of life. It was recently shown that this developing visual ability is boosted by an odor in 4-

month-old infants, neural face categorization being strongly enhanced in the context of mother's body odor. Whether this influence operates until the end of the first year, as face categorization becomes more efficient by itself, must be established. Here, we recorded the electroencephalogram (EEG) of 4- to 12-month-old infants (N = 50) while they were watching streams of rapidly changing pictures (6 pictures/sec leading to a 6-Hz frequency of stimulation) including living and non-living objects. Human faces were periodically inserted once per second (i.e., at 1 Hz). During visual stimulation, infants were also exposed to a T-shirt imbued with maternal odor vs. an unworn, baseline T-shirt. Using a frequency-tagging approach, we reveal that the amplitude of the face-selective neural response tagged at 1 Hz in the EEG spectrum increases with age over the occipito-temporal cortex, marking the development of face categorization. Critically, while the strength of the face-selective response increases as a function of age, the "facilitative" effect of maternal odor decreases over the same time. These results suggest the operation of a developmental trade-off between vision and olfaction and support the view that visual perception relies on odor cues in developing infants until the sole visual system becomes able on its own to readily achieve categorization.

Tue-Posters-032

Odor qualities influence odor identification and naming performance in older adults

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Odor identification (with word cues) and naming (without cues) abilities are often impaired in aging adults. Severe impairment predicts future cognitive impairment, and clinical onset of dementia. Understanding the unique processing demands of the odor identification task is thus of high priority - however, investigations of this kind are sparse. We examined how olfactory-perceptual features that vary among the individual odors in the set, can be used to predict identification and naming performance in older adults. We used data from the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K), where 2479 individuals (age 60-100 years) were assessed for odor identification and naming abilities using the Sniffin' TOM test (a validated, slightly modified version of the original Sniffin' Sticks identification test). In order to derive information about the perceptual differences between the 16 odors, we conducted a psychophysical rating experiment where 37 adult participants rated the pleasantness, intensity, familiarity and edibility of the odors. We also

collected pairwise similarity ratings to establish the relative distinctiveness of the 16 odor qualities. Random effect logistic regression modelling was then used to predict the influence of the perceptual features on odor identification. Results show that the perceived odor intensity was the strongest predictor of identification success in the aging sample. Intensity also correlated significantly with naming and identification ability. Further, in agreement with previous research, unpleasant odors were more easy to identify than pleasant odors - pleasantness was the strongest predictor for naming ability. We conclude that for aging persons, odor identification and naming ability can in part be explained by the perceptual features of the odor. Our research approach can be used to optimize olfactory tests for different clinical conditions. This research was funded by the Swedish e-Science Research Center.

Tue-Posters-033

Use of machine learning algorithms to optimize COVID-19 detection by smell test items

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Despite progress in the development of COVID-19 vaccines, reaching herd-immunity is believed unlikely in many countries due to such factors as vaccine availablity, hesitancy, and emergence of new variants. Among COVID-19's early symptoms is a sudden decrease in smell function which is often unrecognized without objective testing. Thus, practical, sensitive, and inexpensive smell tests may aid in the early identification of COVID-19 patients. To compare the efficacy of 8 machine learning methods for identifying odorant test items sensitive to COVID-19. To develop, using such methods, highly specific, sensitive, and brief parallel olfactory tests that can be sequentially administered with minimal test item remembrance. The 40-item University of Pennsylvania Smell Identification Test (UPSIT®) was administered to 100 COVID-19 patients and 132 healthy controls. Binary UPSIT® item response data were used to train and test machine learning methods, including logistic regression, artificial neural networks, decision trees, and k-nearest algorithms. A simple linear discriminant analysis (LDA) classifier, based on the total number of correct, was also employed. For each model, a sequential feature selection strategy was used to select an initial optimal subset of odorants. To provide tests useful for practical serial testing of COVID-19, an optimization search for multiple sets was performed. LDA) using 29 odorant items achieved the

best overall performance, with an accuracy of 95.7%. Four sets of 8-odorant tests with 91%-93% accuracy were developed that can be used separately or sequentially over multiple days to aid in the early identification of COVID-19. Machine learning algorithms can be employed to optimize the sensitivity and specificity of olfactory tests for identifying patients with COVID-19. We found that a minimum of 8 odorant/response items was needed to achieve high sensitivity and specificity..

Tue-Posters-034

Stepwise connectivity from the human piriform cortex to higher cortical networks

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How is the human olfactory system integrated with central brain networks, and does this integration differ from that of other senses? In this study, we attempt to characterise the profile of connectivity between the piriform cortex and higher areas. To this end, we use a stepwise functional connectivity (SFC) approach developed for fMRI by Sepulcre et al. (2012). The SFC method tracks patterns of functional activity correlations that emerge from seed regions (e.g., primary sensory areas) and unfold in a sequence of connectivity steps. The pathway from a piriform cortex seed was investigated in a sample of 100 healthy adults who underwent resting-state fMRI. In comparison to previous findings in other sensory systems, we found that early olfactory areas are separated by fewer connectivity steps from higher cortical regions. This SFC outcome is in line with previous findings in rodents in which direct projections have been observed between early olfactory areas and regions responsible for high-level cognitive functions. Our results suggest that olfactory centres in the human brain have retained a relatively direct access to higher cortical nodes. Our work helps understand how olfactory information is adaptively transformed across sensory hierarchies to bring about changes required for complex behaviour. The research was funded by the Swedish Research Council (2020:00266) to JKO.

Tue-Posters-035

Binge alcohol drinking after time-restricted exposition to sweet pellets

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Alcohol consumption and sweet substance consumption are strongly associated and appear to share brain mechanisms. In animals, rodents with a high preference for sweet substances consume more ethanol than those with a low preference for these substances. The present study investigates a novel model of voluntary ethanol consumption in which ethanol access follows a time-restriction eating of sweet pellets (59,1% carbohydrate). For this purpose, 61 male Wistar rats were deprived at 82-85% of weight two days before the experiment. For the next 10 days, the animals had access for 3 minutes to either a high amount (72 pellets for experimental condition) or a low amount of sweet reward pellets (6 pellets for control condition). Immediately after that, rats were tested in a two-bottle choice test (duration: 90 min) in which they were exposed to one bottle of ethanol (6% or 10% w/w) and one bottle of water. Rats exposed to a high amount of sweet pellets drank significantly more ethanol in both ethanol concentrations ($F_{6,454} = 13.846$, $p < .001$, $\eta^2p = .27$) than the control condition. Moreover, rats with 10% of ethanol drank significantly more than the 6% ($F_{6,454} = 2.154$, $p < .05$, $\eta^2p = .05$). In additional experiment, alcohol consumption was maintained after adding quinine to 10% of ethanol (0.01, 0.03 and 0.1g/L). The relationship between the taste of ethanol and sweet may play a crucial role on the ethanol intake in this model. The sweet neural pathway seems to be essential on voluntary ethanol consumption; as long as rats sense such taste in ethanol solutions and its suppression produces a reduction of ethanol intake. It is possible that sweet reward pellets stimulate the brain reward pathway and promotes the subsequent consumption of ethanol. Funded by PND-2020-049 (DGPNSD. Ministerio de Sanidad, Spain); FPU18/05012 (Ministerio de Universidades, Spain) and B-CTS-422-UGR18 (Programa Operativo FEDER, Junta de Andalucía)

Tue-Posters-036

Body odor disgust sensitivity predicts odor valence ratings

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Disgust sensitivity to body odors reflect individual differences in disease avoidance and may be a key aspect underlying some social attitudes. The body odor disgust sensitivity scale (BODS) provides a rapid and valid assessment of individual differences. Previous work indicated that BODS

was positively related with ratings of disgust, but not intensity, to sweat biosamples (Liuzza et al., 2017). However, little is yet known about how individual differences in BODS might correlate with odor perception. Here, we investigated how BODS corresponds to perceptual ratings of positively and negatively valenced odors. We aggregated data from 4 experiments (total n=197) that were conducted in our laboratory, and where valence and intensity ratings were collected. Unpleasant odors included valeric acid (sweat-like), butyric acid (vomit-like) and skatole (fecal), odors which may provide disease cues. Pleasant odors included those associated with hygiene (e.g. lilac; a common fragrance in soap). Using Bayesian multilevel modelling we show that individuals with higher BODS levels perceived pleasant smells as more valenced overall: unpleasant smells were rated as more unpleasant, but pleasant smells were rated as more pleasant. Furthermore, we investigated whether overall BODS score or scores one of the two subsets of the scale (i.e. odor source is oneself, vs. someone else) were best at predicting valence ratings. Interestingly, the disgust sensitivity to odors coming from internal sources (e.g. one's own sweat) was the best predictor of odor valence. In sum, high BODS is associated with more extreme odor valence ratings. The monitoring of one's own body odor might have relevance for understanding the role of olfaction and disease avoidance, but more research is needed. This research was supported by the Swedish Research Council (2016:02018) to J.K.O.

Tue-Posters-037

Subjective olfactory decline is associated with future smell loss

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Subjective olfactory decline (SOD), does not correlate well with olfactory performance and is sometimes regarded as an unreliable assessment, yet it is associated with future risk of dementia. Here, we compared SOD with subjective cognitive decline (SCD), which is known to be associated with an increased risk for future cognitive impairment and dementia. We aimed to test whether SOD and SCD are associated with olfactory and/or cognitive performance at 10 years follow-up. We used data from a population-based sample aged 45 to 90 years at baseline (n=307; 52% female). The sample was split into healthy controls (HC), SOD and SCD. General cognitive status (Mini-Mental State Examination) and olfaction (Scandinavian Odor Identification test; SOIT) were assessed in all subjects. We used within-subjects ANOVA for baseline-to-follow-up comparisons and multiple linear regression models for each group at follow-up to test for the association between

objective olfaction and cognition measured with several cognitive test. Individuals with SOD had no olfactory impairment at baseline, but an impairment emerged at follow-up. In this group, SOIT scores at follow-up were positively associated with their cognitive scores. There were no significant associations between cognition and olfaction in the SCD group. Subjective olfactory complaints may indicate subtle olfactory deficits that may later become observable and may also indicate future cognitive status. The research was supported by the Swedish Research Council (2020:00266) to J.K.O.

Tue-Posters-038

Functional interaction between *Drosophila* olfactory sensory neurons and their support cells

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Insects detect volatile chemicals using antennae, which house a vast variety of olfactory sensory neurons (OSNs) that innervate hair-like structures called sensilla, where odor detection takes place. In addition to OSNs, the antenna also hosts various auxiliary cells. These include the triad of trichogen, tormogen and thecogen support cells that lie adjacent to their respective OSNs. The arrangement of OSN supporting cells occurs stereotypically for all sensilla and is widely conserved in evolution. While insect chemosensory neurons have received considerable attention, little is known about the functional significance of the cells that support them. For instance, it remains unknown whether support cells play an active role in odor detection, or only passively contribute to homeostasis, e.g. by maintaining lymph composition. To investigate the functional interaction between OSNs and support cells, we used optical and electrophysiological approaches in *Drosophila*. First, we characterized the distribution of various auxiliary cells using genetic markers. By means of an *ex vivo* antennal preparation and genetically-encoded cation indicators, we then studied the activation of these auxiliary cells during odor presentation. We observed acute responses and distinct differences in Ca^{2+} and K^{+} fluxes between support cell types. Finally, we observed alterations in OSN responses upon thecogen cell ablation. These changes occur in a sensillum-specific fashion, without changes in neuronal resting activity. For example, ab1 OSNs show increased responses, while ab3 OSNs show decreased responses in the absence of thecogen cells. Taken together, these results demonstrate that support cells play an active role in odor processing. Our observations thus suggest that support cells functionally interact with OSNs and may be important for the extraordinary ability of insect olfactory systems to dynamically discriminate between odors in the turbulent sensory landscape of insect flight.

Tue-Posters-039

Investigating cortical readout of temporal codes for olfaction

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Many neural circuits exhibit reproducible sequences of activity that correlate with perception, action, or distinct internal states. Neural sequences lasting on the order of tens to hundreds of milliseconds are proposed to mediate essential cognitive processes including navigation, memory encoding and retrieval, and sensory discrimination. However, the extent to which the temporal structure of these sequences impacts the activity of downstream reader circuits remains relatively unexplored. A key example is in the olfactory system, where odors activate stereotyped spatiotemporal sequences of olfactory bulb (OB) glomeruli. The temporal structure of glomerular activity is thought to convey information about odor quality. However, the sensitivity of populations of neurons in downstream piriform cortex to the precise timing of glomerular sequences is not known. To address this question, we developed methods to perform patterned optogenetic activation of olfactory bulb glomeruli while recording extracellularly from large populations of neurons in piriform cortex (PCx) of the awake mouse. To assess how glomerular sequence timing impacts PCx output, we optogenetically activated sequences of glomeruli and jittered the onset timing of each glomerulus while preserving the overall order and duration of the sequence. We found that ensemble representations in PCx are sensitive to the millisecond timing of these input sequences, suggesting that PCx is highly optimized to distinguish between different temporal input codes. In future experiments, we plan to investigate the circuit mechanisms that support this temporal specificity. These findings will provide novel insights into the computational principles and mechanisms underlying neural sequence readout in cortical circuits. This work is supported by NIH U19-NS112953.

Tue-Posters-040

Food olfactory cues reactivity in individuals with obesity and the contribution of alexithymia

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Obesity has been associated with increased reward sensitivity to food stimuli, but the relationship between food olfactory stimuli and obesity is still poorly understood. This study investigated whether individuals with overweight and obesity exhibit increased liking of food odors and wanting of the relative foods, compared to normal-weight individuals, and whether alexithymia, associated with poor interoception, contributes to altered responsiveness to food. Liking and wanting for food and non-food odors presented with an olfactometer were measured through explicit (self-report ratings) and implicit measures (heart rate and skin conductance) in 23 normal-weight and 20 women with overweight/obesity. Differently from normal-weight women, those with obesity explicitly rated food odors as less pleasant than non-food odors, while at the implicit level, both food and non-food odors were associated with reduced heart rate response, indicating increased perceived pleasantness. Importantly, implicit liking for food odors was higher in women with obesity than normal-weight women. No differences between normal-weight and women with obesity emerged in wanting measures, however, while normal-weight women show higher skin conductance response for food odors than non-food odors, women with obesity did not exhibit differences between the two categories of stimuli. Alexithymia was associated with increased implicit liking and explicit wanting of food odors, in particular in normal-weight women. These findings suggest a dissociation between liking and wanting components of reward sensitivity in response to food odors in individuals with obesity. Moreover, both affective and motivational responses to food reward seem to be affected by alexithymia, an aspect that should be taken into account by future studies evaluating the effect of cue exposure intervention for obesity treatment.

Tue-Posters-041

Third molar extraction has positive long-term effects on objectively-measured taste function

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Third molar (“wisdom tooth”) extraction (TME) can produce, in some persons, taste defects postoperatively via damage to the chorda tympani/lingual nerve. Although the taste deficits reportedly resolve within a year, the long-term effects of TME remain unknown. Objective: To compare, retrospectively, the whole-mouth taste function of 891 subjects who had received TMEs,

on average, more than 2 decades earlier to that of 364 individuals who had not undergone TME. All had been extensively tested for smell and taste function at the University of Pennsylvania Smell and Taste Center over the last 20 years. Experimental Methods: A 40-stimulus whole-mouth liquid identification test incorporating 2 presentations each of 5 different concentrations of sucrose, sodium chloride, citric acid, and caffeine was administered to each subject. The mean test scores of the TME and control subjects were compared using analysis of covariance (age = covariate). Odds ratios were computed from binary logistic regression modeling controlling for the effects of sex and age. Results: Those with histories of TME exhibited better test scores for all 4 taste qualities than non-operated controls (all ps < 0.0001; ORs (95% CI) – Sucrose: 1.67 (1.30, 2.16); citric acid: 1.81 (1.40, 2.34); sodium chloride: 1.49 (1.15,1.93); caffeine: 1.46 (1.13, 1.88). No effect of the time since the TME was evident. In both groups, women outperformed men and taste performance declined with age. Conclusions: Persons who have undergone TME exhibit, on average, better taste function decades after the TME than persons who have not undergone TME. The physiological basis for this improvement is unknown, although it could reflect sensitization of CN VII nerve afferents or the partial release of the tonic inhibition that CN VII exerts on CN IX via central nervous system processes. Funding: Based, in part, on a clinical database that was initiated by NIDCD PO1 DC 00161.

Tue-Posters-042

The anti-inflammatory effect of trans-resveratrol in HGF-1 cells is mediated by the human bitter taste sensing receptor TAS2R50*

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Trans-resveratrol (RSV) and rosmarinic acid (RA) have shown their anti-inflammatory effects in various immune competent cell models via inhibition of lipopolysaccharide (LPS)-induced TNF-α- and IL-6-release in recent data. Additionally, both substances are reported to taste bitter. Therefore, we wanted to deduce their involvement on human bitter taste sensing receptors (TAS2Rs) in the RSV- and RA-evoked anti-inflammatory effect in LPS-treated human gingival fibroblasts (HGF- 1) in culture. Initially, we compared the bitter taste intensity of RSV and RA in a sensory trial with 10

untrained panelists, 90 % rated a 50 ppm RSV in water solution more bitter than 50 ppm RA. The bitterness of RSV was able to be reduced by a mean of 19 % due to the co-administration of 50 ppm bitter masker homoeriodictyol (HED). The greater bitter taste intensity of RSV compared to RA was verified by means in the human gastric cell model (HGT-1 cells), which show a TAS2R-linked proton secretion. Afterwards, the immune-modulatory effect of 100 µM RSV was studied in 10 µg/mL LPS-treated immune competent HGF-1 cells. After 6 hrs of treatment, RSV reduced LPS-induced IL-6 gene expression and release by -46.19 ± 12.67 % and -73.81 ± 10.58 %, respectively. By co-administration of HED, this RSV-evoked effect was abolished. Since qRT-PCR analyses demonstrated a regulation of TAS2R50 in RSV w/o HED treated HGF-1 cells, an siRNA knock-down approach was applied to demonstrated involvement in the RSV-induced reduction of LPS-evoked IL-6 release in HGT-1 cells. Subsequently, a chemical interaction between RSV and LPS was excluded by LC-MS/MS analyses. Furthermore, the molecular mechanism of the interaction between RSV and the TAS2R50 were identified by a putative binding mode and performed by induced-fit docking simulations.

Tue-Posters-043

Facial and behavioral expressions as authentic signals for positive emotions brought from a proven active fragranced cosmetic use.

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The Smell and Taste Lab

Today, well-being is more self-centered. A fragranced cosmetic routine can be a solution to bring positive emotions to users. Different methods exist to measure emotions. Our study aimed to prove active fragrance cosmetic use brought authentical emotions to its users spread to close/broader social circles. 17 active European women,24-48 y.o. Identified beloved/social person also included. Face cream formula with 3 different fragrances; 127cream=no fragrance, 271 cream=well-being anti-stress fragrance, 712cream=existing pleasant fragrance. 271fragrance had proven benefits on behavioral, physiological, psychological levels[8;9,10,11;12] Questionnaires: Self-Assessment Manikin(SAM) daily filled, Geneva Emotional Wheel(GEW), Scale General Well-Being(SGWB) weekly filled. CRYFE™ profiler software and experienced expert. 271cream was more appreciated on the 5 smell criteria vs 2 other creams. Fragrance's intensity, long-lasting after application and skin cream fragrance adequation, significantly better for 271cream. Videos analysis showed some women preferred odorless creams at study beginning, at end study preferred odor creams. The more they used fragranced creams, the more comfortable they felt. After 3 weeks, we observed clear user's emotional congruence for 271cream. SGWB showed 271cream significantly improved

well-being users (p = 0.005). SAM questionnaire showed 271cream increased pleasure. Gender relative effect was noticed (p = 0.0088).Dominance increase before/after study for social person. Psycho-physiological and behavioral methods combination completed by customized profiler approaches, allowed to better understand positive emotions felt by users of a proven active fragranced cosmetic use. Emotions from a donor to a receiver through body odors can be induced. How cosmetics can interact with olfactive chemosensory signals to bring positive emotions to close/broader social circles?

Tue-Posters-044

Electrophysiological characterization of periglomerular cells in the mouse accessory olfactory bulb

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The mouse accessory olfactory system (AOS) plays a central role in the detection of chemosignals during social interactions of conspecifics. Along the accessory olfaction pathway, the first central stage of information processing is the accessory olfactory bulb (AOB), which consists of projection neurons (mitral cells) and local interneurons, i.e., granule cells and periglomerular cells (PGCs). AOB mitral cells receive excitatory synaptic input from vomeronasal sensory neurons in multiple glomeruli. These glomeruli are surrounded by PGCs. While PGCs may serve to attenuate the input strength, their actual physiological function remains unknown. Here, we detail the biophysical properties of PGCs. In order to investigate cell type-specific features, we perform whole-cell patch-clamp recordings from visually identified PGCs in acute slices of the mouse AOB. We analyze passive and active membrane properties, voltage-activated currents, and action potential firing. The results reveal neurons with unique properties and, thus, provide first insights into the physiological characteristics of PGCs in the mouse AOB. Ongoing research will continue to shed light on the physiological principles of sensory processing in the AOB network.

Tue-Posters-045

Olfactory Perception in Relation to the Physicochemical Odor Space

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A growing body of research aims at solving what is often referred to as the stimulus-percept problem in olfactory perception. Although computational efforts have made it possible to predict perceptual impressions from the physicochemical space of odors, studies with large psychophysical datasets from non-experts remain scarce. Following previous approaches, we developed a physicochemical odor space using 4094 molecular descriptors of 1389 odor molecules. For 20 of these odors, we examined associations with perceived pleasantness, intensity, odor quality and detection threshold, obtained from a dataset of 2000 naïve participants. Our results show significant differences in perceptual ratings, and we were able to replicate previous findings on the association between perceptual ratings and the first dimensions of the physicochemical odor space. However, the present analyses also revealed striking interindividual variations in perceived pleasantness and intensity. Additionally, interactions between pleasantness, intensity, and olfactory and trigeminal qualitative dimensions were found. To conclude, our results support previous findings on the relation between structure and perception on the group level in our sample of non-expert raters. In the challenging task to relate olfactory stimulus and percept, the physicochemical odor space can serve as a reliable and helpful tool to structure the high-dimensional space of olfactory stimuli. Nevertheless, human olfactory perception in the individual is not an analytic process of molecule detection alone, but is part of a holistic integration of multisensory inputs, context and experience.

Tue-Posters-046

Olfactory organoids - on the way to a human olfactory epithelium derived from iPSCs

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The development of the human olfactory epithelium (OE) and the whole olfactory system is complex in nature and until now poorly understood, due to its challenging accessibility. The embryonic induction and development of the olfactory placode (OP), which gives rise to the OE, is dependent on complex multilateral tissue interactions, limiting the modeling capacity of classical adherent cell culture. Here, we report first evidence of a human induced pluripotent stem cell (hiPSC) derived olfactory organoid, co-inducing forebrain neuroectoderm, non-neural ectoderm, olfactory placode, and nasal mesenchyme. These structures develop and appear similar to their in vivo counterparts.

The organoids were generated from hiPSC in suspension culture using our optimized differentiation protocol from earlier adherent studies. Directed differentiation towards an olfactory fate was achieved by temporal manipulation of FGF, WNT, BMP, TGFβ, and SSH signaling pathways, mimicking the in vivo situation. Organoids were analyzed using immunostainings as well as qPCR and showed faithful marker expression with a high level of morphological organization. They present with forebrain-vesicle-like structures inside and a surface-like ectoderm on the outside. This surface-like ectoderm is enriched for pre-placodal-region-like cells, which later form thickened placodal patches and invaginate into the bona fide nasal mesenchyme between the surface-like-ectoderm and the telencephalic tissue. We can report the successful and robust differentiation of iPSC into olfactory organoids and further insights into the development of the human OE. Our findings show the possibility to generate organoids with developing OP and possibly even an OE in vitro. Further efforts will need to be made in the future with the goal to generate a functioning in vitro model of the human OE, which will open new possibilities for disease modeling and drug testing. All funding was granted by the University of Tübingen.

Tue-Posters-047

A web-based smell training application for olfactory rehabilitation following COVID-19

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Smell training is an evidence-based method to treat smell loss. However, existing methods for training at home provide little data about day-to-day changes in olfaction and provide limited means to monitor training activities. We developed a web-based smell training application that allows for daily smell training at home. Unlike previous smell training regimens, the web-based application allows tracking of daily performance on several measures related to olfactory functions. Participants with COVID-19 induced anosmia or hyposmia (TDI < 30.75) are currently being enrolled for the smell training program. All participants are assigned to perform a smell training routine 2 times daily for 8 weeks. Each smell training session includes engaging with 10 household odors for 20 seconds each, rating them on pleasantness and intensity. Data collection is ongoing and will continue during the summer and fall of 2021. The application and preliminary empirical results will be presented at the ECRO 2021 conference, focusing on day-by-day fluctuations in olfactory perception during the recovery period. The results will provide new insights into the recovery phase and inform methods development to optimize smell training interventions. The research is supported by the Swedish Research Council (2020:00266) to J.K.O.

Tue-Posters-048

Comparison of methodology to assess odor-taste interactions: visual analog scale vs ranking task

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Odor and taste are integrated by the brain into a unique flavor perception. Odors then acquire the taste property and can enhance the taste intensity. This phenomenon is called Odor-Induced Taste Enhancement (OITE). The most common method to investigate OITE is the Visual Analog Scale (VAS). Taste intensity scales are cognitively demanding and produce a large inter-individual variability. In comparison, the Ranking Task (RT) is easily performed and is less prone to inter-individual variability. Here we compared the VAS and the RT methods to assess sweet and salty OITE in normal-weight (NW) and obese (OB) participants. 41 NW and 44 OB performed the VAS experiment and 43 NW and 28 OB performed the RT experiment. The beverages were apple juice (Aj), sweet water (sucrose), green-pea soup (Gp), and salty water (NaCl). Vanillin and bacon aromas were used to enhance sweetness/saltiness respectively. In the VAS experiment, for each beverage, 3 solutions were prepared: one with only sugar/salt, another with only the aroma, and the last combining sugar/salt with the aroma. Participants rated the sweetness/saltiness, sourness, bitterness and the global aroma intensity. In the RT experiment, participants received 4 bottles, 3 solutions with increasing concentrations of sucrose/NaCl (S1 to S3) for each base (e.g. AjS1, AjS2, and AjS3), and one of the odorant-added solutions (e.g. AjS1+vanillin). Participants had to rank the 4 bottles according to sweetness or saltiness intensity. In the VAS experiment, OITE was found neither in the sweet nor in the salt beverages. In the RT experiment, OITE was observed but differently according to groups and beverages. In the apple juice, OITE was observed only in OB whereas in the green-pea soup it was found for both groups. In sweet or salty water, OITE was found for both groups. To conclude, the RT method is more efficient to assess the OITE in comparison to the VAS. This work was supported by the ISITE-BFC awarded to C Sinding & Firmenich.

Tue-Posters-049

Mouse AOB granule cells display diverse physiological characteristics

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In most mammals, the accessory olfactory bulb (AOB) plays a key role in pheromone detection. The AOB network consists of excitatory projection neurons (mitral cells) and different groups of local interneurons that shape mitral cell activity. Granule cells (GCs) make up the most prominent interneuron type. They are connected to AOB mitral cells by reciprocal dendrodendritic synapses. While GCs play an essential role in AOB information processing, their physiological characteristics remain elusive. Here, we describe GC electrophysiological properties. Using whole-cell patch-clamp recordings in acute brain slices from wild type mice, we investigate cell type-specific features such as membrane properties, ion channel composition, spontaneous activity, and synaptic input. First, passive and active membrane properties differ from GCs in the main olfactory bulb. Moreover, within the AOB GC population, properties are heterogeneous, suggesting the existence of distinct GC subpopulations. Second, recordings reveal expression of voltage-gated potassium, sodium, and calcium channels as well as HCN channels. Third, a subset of cells displays spontaneous action potential firing at moderate frequencies. Finally, AOB GCs receive distinct patterns of synaptic input. Together, this research provides first insight into the physiological characteristics of AOB GCs, indicating diverse roles in AOB information processing.

Tue-Posters-050

Consequences of gaining olfactory function after life-long anosmia - a case study

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The recovery of smell in chronic smell loss patients have been reported in previous case reports; however, we present a rare case in which a patient has gained her smell after life-long anosmia. The case presents a patient who was objectively tested and diagnosed with functional anosmia at age 13 and at age reported they were experiencing a new sensation of smell. Our results clearly show an electrophysiological signal to two unimodal odorants. The patient had a retronasal score in the hyposmic range and self-reported the ability to smell some non-trigeminal odors (e.g., lavender, lilac). However, this appearance of olfactory function after life-long absence appears to have some negative aspects. The patient reported being disturbed by the presence of the new

sense, and also by the co-occurrence of phantosmia or lingering odors. We discuss our case in possible routes of neurogenesis as well and non-forming memory association with odors.

Tue-Posters-051

Dissecting a neural substrate for predator odor-induced analgesia

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Multimodal integration is imperative for an organism to form a coherent representation of its environment to select the appropriate behavior. In multisensory integration, one sensory modality can influence the processing of another. One example of cross-processing of sensory modalities is predator odor-induced analgesia, a type of stress-induced analgesia (SIA). In this model, the predator odor induces a high stress state, and mice subsequently display decreased nociceptive responses, a readout of analgesia. While SIA has been shown to critically depend on the central amygdala (CeA), the circuit mechanisms that underlie the way in which specific odor stimuli modulate pain perception remains unknown. Here we show that the predator odor, 2MT, has an analgesic effect in naïve mice. We confirm that 2MT activates a region of the olfactory pathway called the amygdala-piriform transition zone (AmPir), which was previously reported to mediate the stress response to predator odor (Kondoh et al., 2016). We now show that AmPir sends strong projections to a subpopulation of CeA neurons that are activated by general anesthetics (CeA_{GA}), which have been shown to produce robust analgesia when optogenetically stimulated (Hua et al., 2020). Finally, using both in vivo calcium imaging and cFos expression, we show that CeA_{GA} neurons are activated by 2MT. Thus, we hypothesize that 2MT produces analgesia by activating AmPir neurons which, in turn, activates CeA_{GA}. Future studies aim at dissecting the necessity of the AmPir-CeA circuit in predator-induced analgesia through silencing of CeA_{GA} during exposure to 2MT. These findings will provide novel insights into the neural circuits mediating the interplay between olfaction and pain perception, and advance our understandings of how sensory modalities modulate one another.

Tue-Posters-052

Olfactory habituation during odour imagery and actual odour stimulation.

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The existence of a close similarity between olfactory perception and imagery is still an unsettle issue with research providing controversial results. Here we address the possible perceptual nature of odour imagery by investigating whether there is a similar reduced behavioural response after repeated exposure (habituation) to a real or imagined smell. Twenty-six volunteers took part in this study, half of them had to smell and to imagine a lemon odorant while the other half smelled and imagined a strawberry odorant. In the odour imagery condition, participants had to imagine the same odour 12 times, while in the perceived odour condition they had to smell the same odorant 12 times. In both conditions, participants rated the intensity and pleasantness of the imagined and smelled odour stimuli on each trial. Overall, both odours were rated as equally pleasant, whereas the lemon odour was rated as more intense (78.5 ± 12.3 vs. 71.3 ± 16.0, $p = 0.019$) and trigeminal (40.7 ± 27.3 vs. 17.7 ± 20.7, $p < 0.001$) compared to strawberry. Furthermore, participants reported that the lemon stimulus was closer to their own concept of the smell of lemon compared to strawberry (74.8 ± 23.4 vs. 41.4 ± 30.1, $p < 0.001$). By means of linear mixed-effects models, we found a comparable and significant reduction of perceived intensity and pleasantness over time during both odour imagery and actual odour stimulation. However, this was retrieved for the lemon odour (intensity, $p = 0.993$; pleasantness, $p = 0.228$) but not for strawberry (intensity, $p < 0.001$; pleasantness, $p = 0.023$). Comparable olfactory habituation following imagery and actual odour stimulation could be odour specific and might be associated with the intensity and the trigeminal sensation evoked by the stimuli. It is also possible that these results are driven by how much the target odorants resembled the participants' own olfactory mental representation. This work was supported by the University of Trento.

Tue-Posters-053

Direct and self-reported assessment of chemosensory abilities in Italian individuals affected by long-term COVID-19

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Recent evidence highlights sudden smell and taste loss as early symptoms of coronavirus disease 2019 (COVID-19). Such symptoms persist in the post-acute phase of the disease. Here, we present the initial results of an ongoing longitudinal study aiming to compare the results of at-home direct smell test and self-reported measures over the course of a year (start date: June 2021) in patients

with self-reported long COVID-19. We used the Italian version of the SCENTinel test as direct measure of odor detection, intensity and identification, and the Smell-&-Taste-Check developed by the Global Consortium for Chemosensory Research as self-reported measure of subjective experiences and intensity ratings post-exposure to smell, taste and chemesthetic stimuli. This preliminary cohort includes 49 Italian individuals (expected final N = 400) with long-term sequelae from COVID-19 (mean age = 44.6 ± 11.6, range = 22–63 years old, 76% women, duration of smell/taste symptoms = 260.5 ± 117.6 days, range = 29–577 days). 63.3% of participants meet the criteria of accuracy for SCENTinel. Participants who accurately vs. inaccurately completed SCENTinel did not show shorter symptoms duration ($\beta = -0.001$, SE = 0.001, $z = -0.896$, $p = 0.370$). Responses to the calibrated odor stimulus delivered via SCENTinel highly correlate with the odor intensity collected via household items via the Smell-&-Taste-Check ($r = 0.66$, $p < 0.001$), as well as with self-reported ability ($r = 0.46$, $p = 0.026$). Taste and chemesthesis self-reports and intensity collected via the Smell-&-Taste-Check correlate between each other ($r = 0.50$, $p = 0.016$ and $r = 0.61$, $p = 0.002$, respectively). These preliminary findings need to be corroborated within a larger sample and with longitudinal observations. After completing data collection, we anticipate a significant association between smell ability as assessed via SCENTinel and the duration of symptoms. This work was supported by the University of Trento (project “COG19”).

Tue-Posters-054

Sweet taste receptor-based assay to investigate synergism among sweetener mixtures

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Sweet taste perception is mediated by a single heterodimeric receptor composed of two distinct subunits, called TAS1R2 and TAS1R3 belonging to the class C G protein-coupled receptors (GPCRs). Like other class C GPCRs, TAS1R2 and TAS1R3 subunits share a large N-terminal domain (NTD) linked to the heptahelical transmembrane domain by a short cysteine-rich region. This unique receptor recognizes a wide variety of sweet tasting compounds including natural sugars, synthetic and natural sweeteners. The existence of multiple ligand binding sites on the TAS1R2/TAS1R3 receptor explains the phenomenon of synergy observed between some combinations of sweeteners. The blending of sweeteners is widely used in food products and beverages. For instance, mixtures of saccharin and cyclamate or sucralose and acesulfame-K help to increase sweetness and allow bitter taste reduction. Here, we used functional expression of the human sweet taste receptor using heterologous HEK293 cells and calcium mobilization assays to investigate sweet taste synergism between binary mixtures of 6 sweeteners varying in chemical

structure and type, including neotame, rebaudioside A, rebaudioside M, mogroside V, allulose and the plant sweet-tasting protein, thaumatin. We demonstrated that EC50 values measured for sweeteners alone are correlated to their sweetness potency. Cellular assays revealed that some of the tested binary mixtures were synergistic. These results revealed the usefulness of performing in vitro cellular assay prior to laborious sensory analysis to help to find new solutions for sugar-reduced formulations. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 774293

Tue-Posters-055

Changes in sucrose intake and preference cognitively mediated by an aversive context in rats.

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Cognition seems to play an important role in the development and maintenance of restrictive eating patterns. However, to our knowledge there are not animal models addressing the mechanisms by which thoughts can promote decreased food consumption. In this regard, the present experiments try to fill this gap by exploring the changes in sweet solutions acceptance and preference without the animals ever having experienced physical visceral distress directly but by means of “disgusting” mental representations in both male and female adult Wistar rats. In Experiment 1 we used a second order conditioning protocol (N=32) in which along two repeated cycles drinking a sucrose solution (10%) was paired with a physical context previously associated with unpleasant body rotation. During the test, animals were given access to the sucrose solution in a neutral context and in the home cage. The results showed lower consumption of the sweet solution in the experimental group than in the control group during the first (lowest $F(1,30)=5.15$, $p<.05$, $\eta 2 =.147$). In Experiment 2 we used a mediated conditioning protocol (N=32) in which the animals drank the taste solution in an initially neutral context which was later associated with unpleasant body rotation during six daily sessions. We found similar results to those found in Experiment 1 during the first cycle ($F(1,30)=32.724$, $p<.01$, $\eta 2 =.208$. These results support the role of unpleasant cognitions in modulating sweet food intake and highlight the potential translational value of this protocol for developing animal models of cognitive processes in eating disorders. Funded by PSI2017-86381-P, PID2020-114269GB-100(MINECO, Spain); Marie Sklodowska-Curie Nº 754446 - Athenea3i; and the CTS-1003 research group (University of Granada, Spain).

Tue-Posters-056

Functional molecular switches of mammalian G protein-coupled bitter-taste receptors

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Among the multiple perceptions triggered by the gustatory system, bitterness is usually associated with the avoidance of food and is believed to have evolved to alert us against the consumption of toxic plants. The human genome possesses 25 functional TAS2R genes encoding bitter taste receptors that are differentially activated by a broad range of chemically and structurally diverse bitter compounds. TAS2Rs belong to the G protein-coupled receptor (GPCR) family, and while several GPCR structures have been experimentally solved, the exact tridimensional structure of TAS2Rs has yet to be determined. Without such key structural information, predicting the activity and mechanism of action of bitter molecules on TAS2Rs mostly relies on molecular modeling. Here, we present an integrative computational protocol that combines sequence alignment, homology modeling and constraints derived from site-directed mutagenesis data to build relevant 3D models of all human TAS2Rs. Using TAS2R16 as a test case, we challenged the accuracy of our model by mutating the positions we identified as functional molecular switches involved in ligand sensing and downstream signaling. These results provide molecular insights on structure-function relationships of bitter taste receptors that could be extended to the mammalian repertoire, and layout the groundwork for the development of bitter taste modulators. Funding: French Ministry of Higher Education and Research, UCAJEDI "Investments in the Future" grant number ANR-15-IDEX-01, National Research Foundation of Korea grant number NRF2020R1A2C2004661, GIRACT (Geneva, Switzerland), the Gen Foundation (Registered UK Charity No. 1071026), and support from the Université Côte d'Azur's Center for High-Performance Computing.

Tue-Posters-057

Binding site identification of the highly conserved insect odorant co-receptor (ORco)

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Insects live in an olfactory world, as finding food, mating partners, avoiding predators, or communicating is mostly based on odorant emission and detection. As insects represent a major challenge in our society, both in agriculture (~US$70 billion per year) and healthcare (~US$6.9 billion per year), discovery of chemicals acting on their behaviours is crucial. Insects' olfactory neurons sense chemicals through activation of multimeric ion channels where highly variable odorant receptors are coupled with a conserved co-receptor (ORco). While ORs are sensitive to a large diversity of volatile compounds, only few synthetic agonists are known to activate ORco. To identify the binding site and the ligand diffusion pathway into ORco, multiple molecular dynamics simulations (~20 μs in total) were carried. An ion channel made up of four ORco protomers was embedded into a lipid bilayer and surrounded by several agonists. The simulation analysis provided a rational approach to guide in vivo functional assays. We identified and described the binding pathway through which the insect ORco recognize its ligands. This finding opens the way to the rational design of insect repellents. This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (grant agreement No 682286) and from the Edmond Roudnitska foundation.

Tue-Posters-058

The shape of pleasantness: Using artificial neural networks to derive molecular features relevant to olfactory percepts.

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The olfactory system employs an ensemble of odorant receptors (ORs) to sense molecules in the environment. Molecular features leading to specific olfactory percepts are not fully understood. We argued that olfactory receptors can be viewed as 3D filters that sense a set of molecular spatio-chemical features relevant to olfactory perception. As such, these filters can be represented by neural network used in artificial intelligence algorithms, such as convolutional neural networks. Using large-scale datasets of molecular structures and human olfactory percepts, we trained an artificial neural network called DeepNose to predict human perceptual qualities based on molecules' 3D structures. We designed the structure of our network to represent the information flow in the human olfactory system. Using DeepNose, we can infer the molecular features leading to particular perceptual qualities. Thus, we find that unpleasantness can be traced to well-localized features of molecules. The spatio-chemical definition of pleasantness, on the other hand, is more diverse,

suggesting a non-linear mapping between molecular properties and percepts along the valency axis. Overall, we find a diverse set of definitions for various semantic perceptual qualities and their molecular substrates ranging from well-defined chemical groups and specific spatial shapes to delocalized combinations of chemical features. Our framework helps identify the molecular underpinnings of human olfactory percepts and may facilitate the design of molecules with given qualities.

Tue-Posters-059

Exploring the olfactory neuroecology of *Drosophila virilis*

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Drosophila melanogaster (subgenus Sophophora), a well studies model organism, utilizes fermenting fruits as its substrate, while *Drosophila virilis* (subgenus Drosophila) has evolved to use fermenting tree sap (slime flux) as its primary substrate. Compared to *D.melanogaster*, significantly less information is available about the ecology and evolutionary shifts in *D.virilis* that enables it to utilize a different niche. To understand these major evolutionary changes, we collected tree sap from multiple field sites. In the saps, we identified 80 volatile compounds by using gas chromatographic-mass spectrometric (GC-MS) analysis. Several of the identified odors turned out to be behaviorally active. One compound in particular, 2,6-dimethoxyphenol (syringol) significantly attracted both larval and adult stages of *D.virilis*, while being repellent to *D. melanogaster*. Furthermore, exposure to syringol triggered deposition of droplets containing the aggregation pheromone, (Z)-10-heneicosene, by males. Next, we carried out antennal screening with a panel of 57 compounds using single sensillum recording technique (SSR), and could identify 10 different sensillum classes. In comparison to *D. melanogaster* sensillum types, we did not find an ab3-like sensillum class. Interestingly, it has been reported that the broadly tuned olfactory receptor Or22a, expressed in the ab3 sensillum type in species from the *D. melanogaster* subgroup, is not expressed in *D.virilis*. We also observed a significant overexpression of an ab9-like sensillum class that is characterized by a broad tuning profile. In conclusion, we reveal specific behavior towards sap-related odors and demonstrate that peripheral coding in *D.virilis* is different as compared to *D.melanogaster* with deletions, additions and response changes among sensillum classes.

Tue-Posters-060

Nosewise: a handheld olfactometer for virtual reality olfactory interactions

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The sense of smell, olfaction, is rarely used in digital interactive systems, but, supported by the proper technology, olfaction might open up new interaction domains. Human olfactory experience involves active exploration, directed sniffing and nuanced judgements about odor identity, concentrations and blends, yet most olfactometers are not designed to study these aspects. We present a novel, compact and low-cost olfactometer fitted to the hand controller of the HTC Vive Virtual Reality (VR) system that employs stepless valves to enable control of scent magnitude and blending. Our olfactometer allows for concealed (i.e., unknown to the user) combinations of odors with virtual objects and contexts, making it well suited to applications involving active sniffing and interrogation of objects in virtual space for recreational, scientific, or therapeutic functions. Validation experiments involve gas sensor measurements and a smell training game in a “virtual wine cellar” where participants pick up and smell wine glasses. Results of the gas sensor study demonstrate precise and consistent scent output over extended periods of use. Results from a pilot study with a single normosmic participant using the smell training game for 2h daily over 28 days indicated dramatically increased performance in odor discrimination, identification and naming. An additional study of 12 novice participants provided insights into the usability characteristics of the olfactometer. In sum, our compact, low-cost olfactometer for virtual reality applications is sufficiently robust and exact to enable use in research experiments and game applications, developing expertise, and other olfactory interactions. Our olfactometer enables new forms of multisensory olfactory research where participants interact directly with odorous objects in VR environments. The research was funded by the Marcus and Marianne Wallenberg Foundation (MMW 2014:0178) to J.K.O and S.N.

Wed, 15 Sep -08:30 - 10:30

Symposium 3 - Symposium 3

Wed-S3-001

Sensory detection by Gαi2+ VSNs modulates experience-dependent social behaviors in female mice.

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In mammals, the olfactory system modulates reproductive and socio-sexual behaviors. Olfactory-driven responses may evolve after social experience. For example, pheromone detection induces naïve virgin females to retrieve isolated pups to the nest and to be sexually receptive to males, but social experience increases the performance of both types of innate behaviors. Whether animals are intrinsically sensitive to the smell of conspecifics or detecting olfactory cues modulates experience for displaying social responses is currently unclear. At least two populations of the vomeronasal organ (VNO) sensory neurons detect chemosignals through two families of G-protein-coupled receptors, V1Rs and V2Rs. Here, we employed a conditional knockout mouse for Gαi2 gene, which is required for sensory transduction in apical V1R+ neurons of the vomeronasal organ (Trouillet et al., 2019), to study how pheromone detection and experience-dependent plasticity interact to modulate social behavior. In pup- and sexually-naïve females, Gαi2 deletion elicited a reduction in pup retrieval behavior, but not in sexual receptivity. By contrast, experienced animals showed normal maternal behavior, but the experience-dependent increase in sexual receptivity was incomplete. Altogether, our data suggest that the detection of pheromones by the VNO influences olfactory-mediated behavior in females after social experience, although with distinctive traits for different behaviors. This work was supported by Deutsche Forschungsgemeinschaft, the Region Centre Val de Loire and the NIH Research Program.

Wed-S3-002

Functional characterization of a lineage specific odorant receptor cluster in *Manduca sexta*

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Insect odorant receptors (ORs) expand by gene duplication and divergence in their sequence and function. In the hawkmoth *Manduca sexta*, a recent lineage-specific OR expansion forms a cluster of 5 paralogous MsexOR genes orthologous to one OR of *Bombyx mori*. In this study, we aim to characterise the function of this OR cluster. We hypothesized that these 5 MsexORs have a response profile similar to their orthologue OR in *B. mori*, which responds to esters. We heterologously expressed individual MsexORs in the antennae of the vinegar fly *Drosophila melanogaster*, and electrophysiologically tested olfactory responses to a set of 80 chemically diverse and ecologically relevant odours. We found that the paralogous MsexORs not only respond to esters, but also to some terpenes and aldehydes, showing a broader tuning than their *B. mori* orthologue. The ligands include major volatile components of hawkmoth-pollinated flowers and are known to elicit feeding behaviour in adult *M. sexta*. Odour response profiles of the ORs showed positive correlation primarily with Ca2+ activity of feeding-associated glomeruli in the AL. One of the ORs, MsexOR36 and the feeding-associated glomerulus 12 showed the highest correlation (Spearman r = 0.67, p<0.0001). We also found a positive correlation of MsexOR36 response with odour-evoked proboscis contact duration in wind-tunnel assays (Spearman r =0.28, p=0.012). These results indicate a possible role of these ORs, especially MsexOR36, in feeding. Therefore, we have generated a MsexOR36 knock-out line by CRISPR-Cas9 gene-editing. Using this knock-out line, we aim to understand the role of a single, feeding-associated OR in olfactory perception and behaviour in *M. sexta*. This study was funded by the Max Planck Society.

Wed-S3-003

The genetic and functional basis of olfactory evolution in monogamous and promiscuous deer mice

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Mammals have well-developed olfactory systems and altering the reception of chemosignals can lead to marked modifications of behavior. Yet we still know little about the molecular logic by which biological information is extracted, how this logic evolves, and if it contributes to differences in natural behavior. North American deer mice (genus *Peromyscus*) occupy a wide range of habitats, each with distinct interspecific competitors and predators, as well as highly divergent mating systems, from highly promiscuous to both socially and genetically monogamous. Therefore, deer mice represent an exciting system for studying the genetic mechanisms underpinning complex behaviors and social recognition. Here, we use a reference-quality, chromosome-level *de novo* genome assembly for *Peromyscus maniculatus bairdii* to first show contrasting evolutionary

trajectories between the olfactory and vomeronasal (VNO) subsystems in rodents. While the complements of receptor families expressed in the MOE are largely shared, we found that the receptor repertoire of the VNO differ noticeably. Our comparative genomic analyses reveal that a small set of vomeronasal receptor genes have been preserved in the *Mus* and *Peromyscus* genomes during evolution. These include several receptors for sulfated steroids and bile acids. Next, by focusing on the evolutionary dynamic VNO, we identify genes with high divergence levels in gene expression as candidates for adaptation. Using the activation of these receptors as readouts, we identify pheromone receptors for which differential regulation correlates with the transition between promiscuity and monogamy. Together, our results provide new insights into the evolution of the mammalian olfactory system and identify differences in the olfactory repertoire that likely contribute to adaptation and the transition in the social behaviors of deer mice, opening new avenues for further investigation into the neural mechanisms underlying behavioral evolution.

Wed-S3-004

Sexual isolation between sympatric cactophilic drosophilids

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Sexual isolation is a form of reproductive isolation that prevents gene flow between different taxa. *Drosophila arizonae* is a cactophilic fruit fly with a wide distribution in the deserts of North America. Its range overlaps with its sister species, *Drosophila mojavensis* and another closely related species *Drosophila navojoa*. *D. mojavensis* has been extensively studied in the light of reproductive isolation and it is described as a species complex with four different populations that present different levels of reproductive isolation. However, far less is known about the reproductive behavior of *D. arizonae*. While the four populations of *D. mojavensis* are strict specialists on different cacti plants, *D. arizonae* is a generalist cactus feeder and can often be encountered in sympatry with one of the other species. For this reason, the scope of this study is to unravel the mechanisms involved in reproductive isolation of *Drosophila arizonae*. Among other cues fruit flies use chemical and auditory signals to distinguish suitable mates. Here, we investigate whether forced crosses between *D. arizonae* and the other cactophilic flies result in fertile offspring, and whether the flies use olfactory and/or auditory signals to circumvent hybridization.

Wed-S3-005

Automated quantification of olfactory neuron outgrowth in heterogenous cell cultures

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Olfactory sensory neurons (OSN) regenerate throughout life. Their renewal depends on the cellular architecture of the surrounding tissues and the molecular environment. As a consequence, in-vitro models to characterize OSN regeneration are often based on bulky olfactory epithelium (OE) biopsies or heterogenous cell cultures. To accurately quantify them, fluorescent OSN are usually manually traced to better discern each axon from other structures present in the culture. However, this manual procedure is time-consuming and prone to interpretation bias. To overcome this gap, we developed a specific and entirely automated neuronal growth quantification tool based on a MATLAB script operating on pictures of β-3 Tubulin stained OE biopsies. As a first step, the script enhances the contrast of the picture and detects the biopsy edges. These are used as a starting point to quantify axonal length. Only β-3 Tubulin positive pixels forming a tubular shape compatible with an axon radiating from the biopsy perimeter, are quantified using an algorithm called Fibermetric.The program reports the results (e.g. total axonal length, surface area of the biopsy) in an Excel file. Furthermore, it generates images of the processing steps and a scheme representing the probability of finding an axon at a given angle and distance relative to the biopsy. The comparison between automated and manual axonal quantification showed an intra class correlation coefficient (ICC) of 0.96 (p= 0.017). Furthermore, manual tracing took on average 23 minutes per each explant while the tool average computation time was 3 minutes. The script revealed itself significantly faster than the manual tracing (p= 0.0020). In conclusion, the new automated quantification tool provides an accurate, objective and time-saving method to measure OSN axonal outgrowth. It may facilitate high-throughput screens of regenerative compounds in the future. The project was founded by: Fondation Louis-Jeantet, Auris, Sir Jules Thorn.

Wed-S3-006

SCENTinel 2.0 rapidly screens for quantitative and qualitative olfactory disorders

Mackenzie Hannum [1], Robert Pellegrino [1], Stephanie Hunter [1], Maureen O'Leary [1], Nancy Rawson [1], Danielle Reed [1], Pamela Dalton [1], Valentina Parma [1, 2]

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The COVID-19 pandemic highlights more than ever the need for accurate, reliable and rapid smell testing on a large scale. SCENTinel – a 2-min smell test – was recently developed to assess odor detection, odor intensity, and odor identification ability, discriminating anosmia from normosmia. Here, we assess whether SCENTinel can discriminate quantitative smell dysfunction, including hyposmia, and qualitative smell dysfunction (e.g., parosmia, phantosmia). To enable improved discrimination for qualitative smell dysfunction, we incorporated a new module: odor hedonic perception. A large sample of participants (N=370) were a priori divided as follows: qualitative smell dysfunction (self-report only parosmia/phantosmia, N=86), quantitative smell dysfunction (report only anosmia/hyposmia, N=144), mixed (report both qualitative and quantitative smell dysfunction, N=107), and normal smell function (N=33). Using machine learning techniques, a SCENTinel model can discriminate quantitative vs. qualitative smell dysfunction with high accuracy (0.81 AUROC). Via exploratory analyses, we additionally tested whether SCENTinel can discriminate anosmia from hyposmia and parosmia, by considering a subset of participants who only reported one type of smell dysfunction (N=244). SCENTinel can discriminate anosmia from hyposmia (0.93 AUROC), anosmia from parosmia (0.92 AUROC), and hyposmia from parosmia (AUROC 0.83). We conclude that SCENTinel is a rapid smell test that can be used to screen for quantitative and qualitative smell dysfunction. This research was supported by NIH RADx-rad initiative U01 DC019578 and T32 DC000014.

Wed-S3-007

Host plant constancy in ovipositing *Manduca sexta*

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Insects face complex blends of odors and various color spectrums from their host and non-host plants. To choose an oviposition site, the insects, hence, utilize a combination of visual, olfactory, and gustatory senses. From feeding behavior it is known, that nectar-feeding insects generally target those flower species that they have already experienced as they obviously associate olfactory and/or visual cues from those flowers with the nectar reward they gained. This experience-dependent change of foraging preference is called “flower constancy”. Various studies have shown that flower constancy might benefit an insect by reducing its handling cost. At the same time, flower constancy benefits the plants as it guarantees pollen transfer to flowers from conspecifics. The tobacco hawkmoth *Manduca sexta* is a crepuscular insect that both rely on olfactory cues and visual cues for locating flowers as well as potential host plants for oviposition. In this study we show that *Manduca* females exhibit oviposition constancy, i.e. they prefer host plants they have already

oviposited on. We further investigate, whether the moth profit from this experience-based change in preference and how long they remember the host plant they have experienced already.

Wed, 15 Sep -11:00 - 12:30

Symposium 4 - Symposium 4

Wed-S4-001

Gut-hypothalamic nutrient sensing

Amber Alhadeff

Monell Chemical Senses Center, Department of Neuroscience, University of Pennsylvania

Food intake is tightly regulated by complex and coordinated gut-brain interactions. While we know some mechanisms through which the gut communicates with the brain, our understanding of how nutrients impact in vivo neural activity is in its infancy. In our recent work, we discovered the ability of nutrients in the gut to rapidly modulate neural activity in a small population of hunger-sensitive, hypothalamic neurons expressing agouti-related protein (AgRP). Fat, sugar, or amino acids alone are each capable of inhibiting AgRP neuron activity. How are these nutrients in the gut signaled to the brain to update nutritional status in real time? Because individual macronutrients engage specific receptors in the gut to communicate with the brain, we reasoned that macronutrients may utilize different pathways to reduce activity in AgRP neurons. Indeed, we find site-specific differences in intestinal detection of distinct macronutrients by AgRP neurons. We explore the relative roles of vagal, hepatic portal, and spinal afferent signaling in the regulation of AgRP neuron activity and food intake, and demonstrate that different gut-brain pathways can mediate effects of fat vs. sugar on hypothalamic neuron activity. Further, the inhibition of AgRP neuron activity by the post-ingestive effects of macronutrients is almost perfectly correlated with food intake reductions, suggesting that AgRP neuron activity is a strikingly accurate predictor of feeding behavior. Since AgRP neurons drive food intake, engaging these endogenous inhibitory regulators of hunger circuits may inform new and effective weight loss strategies.

Wed-S4-002

Diet-Induced taste plasticity: causes, consequences, and molecular mechanisms.

Monica Dus, Anoumid Vaziri, Christina May, Hayeon Sung

Department of Molecular, Cellular, and Developmental Biology, The University of Michigan, Ann Arbor, MI

There is a reciprocal interaction between diet and the chemical senses: sensations shape our dietary patterns, and diet, in turn, influences the way we sense food. Indeed, human and animal studies have shown that diet composition can regulate taste sensation and perception, but the causes and consequences of this chemosensory plasticity are still poorly understood. Over the last five years we have used the simple taste apparatus of the fly D. melanogaster to understand the molecular and neural mechanisms of diet-induced taste plasticity. We discovered that nutrients can directly regulate the responses of the taste cells and sensory neurons to sweetness via epigenetic mechanisms, and that chemosensory alterations change meal size and intake by affecting the central processings of sensory information by dopaminergic neurons. We will summarize these findings and present new data showing how a high-sugar diet induces lasting synaptic and morphological changes in the sensory neurons to blunt their output and dull behavioral responses to food.

Wed-S4-003

Reward-related gustatory and psychometric predictors of weight loss following bariatric surgery: a multicenter cohort study

Gabriela Ribeiro [1, 2], Marta Camacho [1], Ana B Fernandes [1, 3], Gonçalo Cotovio [1, 3, 4], Sandra Torres [5, 6], Food Reward in Bariatric Surgery Portuguese Study Group [1], Albino J Oliveira-Maia [1, 3, 4]

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Background: Reward sensitivity has been proposed as a potential mediator of outcomes for bariatric surgery. Objectives: We aimed to determine whether gustatory and psychometric measures of reward-related feeding are predictors of bariatric induced weight loss. Methods: A multicenter longitudinal cohort study was conducted in patients scheduled for bariatric surgery (surgical group),

assessed at baseline and 2 follow-up assessments. Predictions of % weight loss from baseline (%WL) according to baseline gustatory measures, including intensity and pleasantness ratings of sweet and other tastants, and psychometric measures of reward-related feeding behavior, including hedonic hunger scores, were assessed with multivariable linear regression. Exploratory analyses were conducted to test for associations between %WL and changes in gustatory and psychophysical measures, as well as for comparisons with data from patients on the surgery waiting list (control group). Results: We included 212 patients, of whom 96 in the surgical group and 50 in the control group were prospectively assessed. The groups were similar at baseline and, as expected, bariatric surgery resulted in higher %WL. While variation in gustatory measures did not differ between groups, in the surgery group baseline sweet intensity predicted %WL at the primary endpoint (11 to 18 months postoperatively), as did hedonic hunger scores. Furthermore, at this endpoint, postsurgical reduction of sweet taste intensity and acceptance of sweet foods were associated with %WL. The use of sweet intensity as a predictor of weight change was confirmed in another bariatric cohort. Conclusions: Sweet intensity ratings and hedonic hunger scores predict %WL after surgery. The variability of sweet intensity ratings is also associated with %WL, further suggesting they may reflect physiological processes that are variably modulated by bariatric surgery, influencing clinical outcomes.

Wed-S4-004

Genome-wide association study of food liking in 162,000 people uncovers the genetic bases of food liking.

Sebastian May-Wilson [1], Nana Matoba [2, 3], Kaitlin Wade [4], Maria Pina Concas [5], Jouke-Jan Hottenga [6], Massimo Mangino [7, 8], Maria G. Veldhuizen [12], Cristina Menni [8], Eco de Geus [6, 10], Paolo Gasparini [5, 9], Nicholas J Timpson [4], James F. Wilson [1, 11], Nicola Pirastu [1]

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Variable preferences for different foods are among the main determinants of their intake and are influenced by many factors, including genetics. Despite considerable twins' heritability, studies aimed at uncovering food-liking genetics have focused mostly on taste receptors. Here, we present the first results of a large-scale genome-wide association study of food liking conducted on 161,625 participants from UK Biobank. Liking was assessed over 139 specific foods using a 9-point hedonic scale. After performing GWAS, we used genetic correlations coupled with structural equation modelling to create a multi-level hierarchical map of food liking. We identified three main dimensions: high caloric foods defined as "Highly palatable", strong-tasting foods ranging from alcohol to pungent vegetables, defined as "Learned" and finally "Low caloric" foods such as fruit and vegetables. The "Highly palatable" dimension was genetically uncorrelated from the other two, suggesting that two independent processes underlie liking high reward foods and the Learned/Low caloric ones. Genetic correlation analysis with the corresponding food consumption traits revealed a high correlation, while liking showed twice the heritability compared to consumption. For example, fresh fruit liking and consumption showed a genetic correlation of 0.7 with heritabilities of 0.1 and 0.05, respectively. GWAS analysis identified 1401 significant food-liking associations located in 173 genomic loci, with only 11 near taste or olfactory receptors. Genetic correlation with morphological and functional brain data (33,224 UKB participants) uncovers associations of the three food-liking dimensions with non-overlapping, distinct brain areas and networks, suggestive of separate neural mechanisms underlying the liking dimensions. In conclusion, we created a comprehensive and data-driven map of the genetic determinants and associated neurophysiological factors of food liking beyond taste receptor genes.

Wed, 15 Sep -14:00 - 15:45

Symposium 5 - Symposium 5

Wed-S5-001

Neural control of Drosophila foraging and food ingestion

Nilay Yapici, Xinyue Cui

Cornell University, Department of Neurobiology and Behavior

Precise regulation of food intake is essential for every animal to survive. Here, we use the fly, Drosophila melanogaster, to identify food intake and foraging circuits from sensory input to motor output to understand the neural computations the brain uses while deciding to consume a particular food source. We have developed an automated system called Visual Expresso to capture fly foraging and food intake behaviors. This system captures fly locomotion and the dynamics of food intake at high temporal resolution. Visual Expresso data shows that flies regulate their food intake and foraging based on their hunger state and the quality of the food presented. Moreover, we found that hunger and thirst states interact to determine the amount of water or sugar ingested. We are also working on identifying food intake circuits in flies. Previously, we identified a novel class of excitatory interneurons (IN1) in the fly brain that regulates food ingestion. Recently, we focused on identifying the IN1 food intake circuitry using optogenetics and anterograde trans-synaptic circuit tracing. In these experiments, we first focused on identifying sensory and modulatory inputs to IN1 neurons. We have found that sugar sensing neurons that express Gr64f and Gr43a provide excitatory input to IN1 neurons, whereas the other 2 groups of sugar sensing neurons Gr64a and Gr5a, bitter sensing neurons Gr66a, and water sensing neurons ppk28 cannot significantly activate or inhibit IN1 neurons. Neurons expressing the Gr43a receptor generated a strong and sustained calcium response in IN1 neurons thus we further investigated which Gr43a neurons produce this excitatory effect. Using genetic tools available, we labeled different populations of Gr43a neurons and found that a population of gut sensory neurons is required for IN1 activation. We will present our current results and the model for how the gut-brain axis might regulate state-dependent food intake in flies.

Wed-S5-002

Mapping the sensorimotor connectome underlying protein-specific appetites in *Drosophila melanogaster*

Ibrahim Tastekin [1], Rory Beresford [1], Nils Otto [2], Georgia Dempsey [2], Ana Paula Elias [1], Celia Baltazar [1], Raquel Barajas Azpeleta [1], Dennis Goldschmidt [1], Scott Waddell [2], Carlos Ribeiro [1]

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Dietary amino acids are key determinants of lifespan and fecundity. Fruit flies achieve a balanced intake of amino acids under diverse physiological conditions by developing a protein-specific appetite. The *Drosophila* feeding motor program comprises behavioral modules (feeding bursts and activity bouts) which are tightly regulated by physiological states through feedback (e.g. nutrient deprivation) and feedforward (e.g. mating) mechanisms. Here, we aim to understand the neural-circuit mechanisms underlying physiological state-specific regulation of food intake by dissecting

the functional and temporal relationships between protein deprivation and feeding as well as the underlying neural circuits. We discovered that there are temporal differences between regulating the frequency and the duration of feeding bursts, suggesting that distinct neuromodulatory mechanisms modulate these parameters. Different sensory neuron populations control frequency and duration of feeding bursts suggesting that distinct sensorimotor pathways regulate these feeding motor programs. We combined connectomics and trans-synaptic labeling to map neurons downstream of a group of gustatory receptor neurons (taste peg GRNs) that are important for sustaining feeding on proteinaceous food. High-resolution behavioral analysis and optogenetics confirmed the identity of a group of interneurons that specifically regulate the duration of feeding bursts in a nutrient-specific manner, suggesting different aspects of the feeding motor program are controlled by separate circuits.

Wed-S5-003

Hunger enhances food odor attraction in mice

Nao Horio, Stephen Liberles

Howard Hughes Medical Institute, Department of Cell Biology, Harvard Medical School, Boston, MA, USA.

Hunger is a powerful motivational state that intensely drives behaviors predictive of food consumption. However, mechanisms by which internal state shapes olfactory circuits remain poorly understood. Here, by using a simple and robust two-choice assay to investigate hunger dependent odor responses and optogenetic methods, we identified a neuronal mechanism by which hunger enhances attraction to food odors over other olfactory cues. By activating each axon of agouti-related peptide (AGRP) neurons, we found that AGRP neurons promote food odor attraction through projections to the paraventricular thalamus. Studies with KO mice and agonist/antagonist injections showed that food odor attraction by AGRP neurons act through Neuropeptide Y and its receptor NPY5R. We uncovered molecular features that are essential for one such neuromodulatory pathway, as NPY from AGRP neurons opens a thalamic hunger gate for specific olfactory inputs that carry an NPY5R encryption. More generally, these studies provide insight into how internal state guides olfactory behavior. All animal procedures followed the ethical guidelines outlined in the National Institutes of Health Guide for the Care and Use of Laboratory Animals, and all protocols were approved by the Institutional Animal Care and Use Committee (IACUC) at Harvard Medical School.

Wed-S5-004

The role of GnRH3 neurons in modulating olfactory computations and odor induced feeding behaviors

Pradeep Lal, Emre Yaksi

Kavli Institute for Systems Neuroscience, NTNU

Animals can respond differently to a sensory stimulus depending on its internal state (e.g. satiety/hunger). Neuromodulators are crucial in modulating the internal state of the animal. Gonadotropin-releasing hormone (GnRH) is a conserved neuropeptide and, modulates feeding and reproductive behaviors. It is produced by discrete neuronal populations located in the terminal nerve region of olfactory bulb (OB) and hypothalamus and is dispersed widely throughout the brain. Studies suggest that GnRH modulates the basal olfactory response by altering the synaptic properties of olfactory receptor neurons. However, the specific role of GnRH neuromodulation in olfactory information processing is not well understood. To address this, first, we created a transgenic zebrafish line that labels the terminal nerve GnRH3 neurons with Gal4 transactivator and expressed a genetically encoded calcium indicator (GCaMP6s) in GnRH3 neurons. We imaged their activity by using two-photon microscopy and observed that GnRH3 neurons exhibit a high level of ongoing spontaneous activity. We showed that these neurons respond to a diverse set of olfactory stimuli and with strong preference for food related odors. Next, we found that genetic ablation of these neurons led to a significant decrease in feeding and food odor induced behavior. Moreover, this manipulation also led to decrease in food odour reponses in OB neurons. Finally, by optogenetic manipulation, we showed that these neurons modulate spontaneous activity of OB neurons suggesting a basal modulation of OB neural activity by GnRH3 neurons. Thus, our results suggest a central role for the GnRH neuromodulation in the regulation of OB activity, odor coding and olfactory behaviors.

Wed-S5-005

Should I stay or should I go: A response sign switch in a single olfactory neuron switches olfactory preference behavior

Munzareen Khan [1], Anna Hartmann [1], Michael O'Donnell [1, 2], Madeline Piccione [1], Pin-Hao1 Chao [1], Noelle Dwyer [3], Cornelia Bargmann [4], Piali Sengupta [1]

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Animals continuously encounter heterogenous mixtures of multiple chemicals that fluctuate in their concentrations and temporal properties, and inform them of the presence and location of food, mates, competitors, and predators. To correctly decode this information, chemosensory responses must not only be robust and sensitive, but must also be highly flexible. Animals integrate information such as internal state and contextual cues in order to modulate their responses even to cues that are innately attractive (such as those from food), or aversive (such as those from toxic substances). Using high-resolution microfluidics behavioral assays and in vivo calcium imaging, we describe a mechanism by which C. elegans switches its behavioral preference for a subset of food-related odors from strong attraction to strong repulsion based on odorant context. We find that this behavioral switch is driven by a switch in the sign of the response to these odorants in a single olfactory neuron type, and identify signal transduction molecules that mediate this response plasticity. Our results indicate that a food-related chemical can evoke bidirectional sensory responses and drive behavioral plasticity via context-dependent engagement of distinct intracellular signaling pathways in a single sensory neuron type. Funded by the NSF.

Wed, 15 Sep -16:15 - 18:00

Symposium 6 - Symposium 6

Wed-S6-001

Connecting the brain to the gut

Maya Kaelberer

Duke University

Functional gastrointestinal (GI) diseases are the most common diagnoses in gastroenterology. Such disorders, like irritable bowel syndrome or functional dyspepsia, are recognized by altered GI sensitivity, GI motility, and behavior. Though the pathophysiology is complex, a conserved feature is the bidirectional alteration in brain-gut signaling. Thus, these are classified as disorders of brain-gut interaction. While the vagus nerve is the main brain-gut link, almost nothing is known about how the vagus nerve modulates GI epithelial sensory function. In the gut, luminal stimuli are sensed by enteroendocrine cells. Besides their endocrine function, we found that these cells also form glutamatergic synapses with vagal neurons to transduce sugar stimuli to the brain in milliseconds. These innervated enteroendocrine cells are referred to as neuropod cells. Upstream of this circuit, we found vagal neurons innervating the intestine that project to areas controlling motivation and

reward. These findings revealed a possible efferent (brain-to-gut) neural circuit through which the brain could modulate gut sensory processing.

Wed-S6-002

A model of full-length RAGE in complex with S100B sheds new light on the signal transduction mechanism

Kamil Steczkiewicz [1], Alexander Moysa [1], Dorota Niedziałek [1], Dietmar Hammerschmid [2, 3], Lilia Zhukova [1], Frank Sobott [3, 4], Michal Dadlez [1]

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The Receptor for Advanced Glycation End-products (RAGE) is an immunoglobulin-type multiligand transmembrane protein expressed in numerous cell types. For instance, RAGE interaction with S100B leads to RAGE upregulation and initialization of a spiral proinflammatory associated with different neural disorders. The main goal of the presented project was to provide a comprehensive understanding of the structure of RAGE-ligand complexes and to explain the molecular mechanism of signal transduction by this receptor. By combining mass spectrometry-based methods, namely hydrogen-deuterium exchange, cross-linking analysis and native MS, available X-ray structural data, molecular dynamics and integrative molecular modelling we present a structural characterization of the hetero-oligomeric complex of the full-length RAGE with S100B. Our results show that RAGE functions as a tetramer exposing an extensive surface formed by V domains with shape and electrostatics charge suited for efficient S100B binding. Furthermore, HDX results demonstrate an allosteric coupling of the distal extracellular V-domains and the transmembrane region, indicating a possible mechanism of signal transmission by RAGE across the membrane. Our model provides an insight into RAGE-ligand interactions, providing a basis for the rational design of the therapeutic modifiers of its activity. This research was funded by EU CEPT (POIG.02.02.00-14-024/08-00), Foundation of Polish Science TEAM TECH CORE FACILITY/2016-2/2, National Multidisciplinary Laboratory of Functional Nanomaterials (POIGT.02.02.00-00-025/09-00), National Science Centre, Poland MAESTRO (2014/14/A/NZ1/00306) and OPUS (2018/31/B/ST4/03809), POL-OPENSCREEN (DIR/WK/2018/06) from Ministry of Science and

Higher Education, Antwerp University Research Fund for the Concerted Research Actions grant (BOF-GOA 4D protein structure) and Wellcome Trust multi-user equipment grant 208385/Z/17/Z. This research was supported by PLGrid Infrastructure.

Wed-S6-003

Glucose and lipid metabolism regulation: the carotid body-brain magic circuit

Silvia Conde

CEDOC, NOVA Medical School, Faculdade de Ciências Médicas

The carotid bodies (CBs) are peripheral chemoreceptors, classically defined as O2 sensors, but now looked as metabolic sensors involved in carbohydrates and lipid metabolism. Recently, we demonstrated that CBs activity is increased in metabolic disease animals and in prediabetic patients and that the resection of the carotid sinus nerve (CSN), the nerve that links the CB to the brain, prevented and reversed the metabolic alterations induced by hypercaloric diets. Also, CSN resection normalized the sympathoadrenal overactivity present in dysmetabolic states, meaning that the beneficial effects of decreasing CB activity are modulated by target-related efferent sympathetic nerves, through a reflex initiated in the CBs. Insulin, leptin, GLP1 and pro-inflammatory cytokines activate the CB. The present talk will provide a state-of-the-art update on the mechanisms of chemosensory transduction, neural circuitry, and reflex regulation of CBs chemoreceptor in metabolic diseases and will discuss the recent findings that disclose the brain regions involved in CB-dependent metabolic control to complete the circuit between CB-brain-peripheral tissues in the scenario of metabolic disorders.

Wed-S6-004

Developmental origins of homeostatic sensing

Marcelo Dietrich

Laboratory of Physiology of Behavior, Department of Comparative Medicine, Yale School of Medicine, New Haven, CT, USA., Department of Neuroscience, Yale School of Medicine, New Haven, CT, USA., Yale Center for Molecular and Systems Metabolism, Yale School of Medicine, New Haven, CT, USA.

All mammals transition from breastfeeding to independent feeding during the lactation period. In humans and other mammals, this critical transition is important for later in life metabolic control and,

consequently, for the development of many chronic conditions. Here, Dr. Dietrich will discuss the work of his lab studying the function of hypothalamic neurons involved in homeostatic control during the transition from breastfeeding to independent feeding. His work illuminates novel properties of hypothalamic neurons in early life, suggesting mechanisms by which early life events shape homeostatic regulation throughout the individual's lifespan.

Wed-S6-005

Does the gut feel touch?

Arthur Beyder

Mayo Clinic

The gastrointestinal (GI) tract extracts nutrients from ingested meals. In addition to nutrients, meals contain toxins and infectious agents. Consequently, most animals conduct the entire digestive process within the GI tract, but luminal contents are entirely outside the body, separated by the tightly sealed GI epithelium. Therefore, like skin and oral cavity, the gut must sense the chemical and physical properties of luminal contents to optimize digestion and nutrient absorption. Yet, physical sensing of luminal contents remains unclear. The gut epithelium contains specialized sensory enteroendocrine cells (EECs) that intimately interact with luminal contents. We focus on a subpopulation of EECs that have similarities to the light touch sensors in the skin, the Merkel cells. These gut touch sensors endow the gut with an ability to detect small luminal forces and luminal contents' physical properties to regulate critical aspects of GI physiology, suggesting that the gut has a built-in tactile sensing system.

Wed, 15 Sep -18:00 - 19:00

Posters - Poster Session

Thu, 16 Sep -08:45 - 10:30

Symposium 7 - Symposium 7

Thu-S7-001

Assessment of odor hedonic perception: the Sniffin` Sticks Parosmia Test (SSParoT)

David T. Liu [1], Antje Welge-Luessen [2], Gerold Besser [1], Christian A. Mueller [1], Bertold Renner [3, 4]

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Objectives: Qualitative olfactory dysfunction is characterized as distorted odor perception and can have a profound effect on the quality of life of affected individuals. Parosmia and phantosmia represent the two main subgroups of qualitative impairment and are currently diagnosed based on patient history only. We have developed a test method that measures qualitative olfactory function based on the odors of the Sniffin` Sticks Identification subtest. The newly developed test is called Sniffin` Sticks Parosmia Test (SSParoT). SSParoT uses hedonic estimates of two oppositely valenced odors (pleasant and unpleasant) to assess hedonic range (HR) and hedonic direction (HD), which represent qualitative olfactory perception. HR is defined as the perceivable hedonic distance between two oppositely valenced odors, while HD indicates the overall hedonic perception of odors. **Experimental methods:** This multicenter study enrolled 162 normosmic subjects in four consecutive experiments and three patients with qualitative olfactory dysfunction. Cluster analysis was used to group odors from the 16-item Sniffin' Sticks Identification test and 24-additional odors into clusters with distinct hedonic properties. Normative values were derived from normosmic subjects aged between 18 and 35 years. **Results:** Eleven odor pairs were found to be suitable for the estimation of HR and HD. Analysis showed agreement between test-retest sessions for all odor pairs. Preliminary results from two patients with parosmia and one patient with phantosmia provide evidence for the proof of concept of SSParoT. **Conclusion:** SSparoT might emerge as a valuable tool to assess qualitative olfactory function in health and disease. *Funding:* None.

Thu-S7-002

A potential diagnostic tool for olfactory dysfunction: Entropy

Çağdaş Güdücü

Dokuz Eylül University, Faculty of Medicine, Department of Biophysics, Balçova, Izmir, Turkey

Many years of been research on olfactory dysfunction, various techniques have been used and proposed for the diagnosis. Besides the psychophysical evaluation, chemosensory event-related

potentials are one of the leading diagnostic tools for the olfactory dysfunction. However, those techniques have major limitations, and the clinicians mostly struggle to diagnose the olfactory dysfunction of the patients. Therefore, an unbiased tool is needed to enhance the diagnosis of olfactory dysfunction. Entropy is a technique to measure the complexity of EEG signals during the presentation of a stimulus. This complexity may reflect the neuronal activity more precisely than the classical EEG techniques (time-amplitude and time-frequency measurements). So, in this talk, the entropy analysis will be being presented for the possible tool for the diagnosis of olfactory dysfunction. Also, previous studies and ongoing modifications on those methods will be discussed.

Thu-S7-003

New methods to evaluate taste and smell worldwide

Danielle Reed

Monell Chemical Senses Center

The pandemic has accelerated our progress in developing new methods to test taste and smell worldwide. Innovations include conducting supervised sensory testing via Zoom, using unsupervised computer surveys, or doing tests by mail, with postcards that can be self-administered online. A future vision would be a single standardized taste and smell test adopted as a clinical standard in medicine worldwide, similar to hearing and vision tests. The lack of a universal standing makes it hard to compare the results from the over 250 studies of people tested for taste and smell loss with COVID-19 because it is difficult to know if study-to-study differences are due to testing methods or other variables. As a step toward this vision, a recent mailout study of adults of different ancestry illustrates those bitterness intensity ratings collected via Zoom match expectations from their underlying genotype, a data quality control of the worldwide sensory data. New organizations like the Global Consortium of Chemosensory Research have advanced chemosensory testing by quickly translating tests into many languages, further supporting this vision. Challenges to this vision are numerous. They include the costs of stimuli, distributing them promptly and efficiently, the need to have odorants that are familiar to all people, maintaining sensory stimuli concentrations and storage in different environments, and ensuring that participants follow testing instructions. Surmounting these challenges is possible but will require cooperation among the many interested in developing and implementing these standards.

Thu-S7-004

Olfactory bulb investigation in Parkinson's disease and olfactory dysfunctions

Cécilia Tremblay [1, 2], Jie Mei [2], Geidy Serrano [1], Johannes Frasnelli [2], Thomas Beach [1]

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Background: The olfactory bulb is one of the first regions of insult in Parkinson's disease (PD), consistent with the early onset of olfactory dysfunction. Investigations of the olfactory bulb may, therefore, help early pre-motor diagnosis. We aimed to investigate olfactory bulb and its surrounding regions in PD-related olfactory dysfunction when specifically compared to other forms of non-parkinsonian olfactory dysfunction (NPOD) and healthy controls. Methods: We carried out MRI-based olfactory bulb volume measurements from T2-weighted imaging in scans from 15 patients diagnosed with PD, 15 patients with either post-viral or sinonasal NPOD and 15 control participants. Further, we applied a deep learning model (convolutional neural network; CNN) to scans of the olfactory bulb and its surrounding area to classify PD-related scans from NPOD-related scans. Results: Compared to controls, both PD and NPOD patients had smaller olfactory bulbs, when measured manually (both $p < .001$) whereas no difference was found between PD and NPOD patients. In contrast, when a CNN was used to differentiate between PD patients and NPOD patients, an accuracy of 88.3% was achieved. The cortical area above the olfactory bulb which stretches around and into the olfactory sulcus appears to be a region of interest in the differentiation between PD and NPOD patients. Conclusion: Measures from and around the olfactory bulb in combination with the use of a deep learning model may help differentiate PD patients from patients with NPOD, which may be used to develop early diagnostic tools based on olfactory dysfunction.

Thu-S7-005

Parosmia: Prevalence, duration and impact in a population-based, prospective study spanning 10 years

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Parosmia, experiences of distorted smell sensations, is a common consequence of covid-19. Parosmia is not well understood in terms of its impact and long-term outcomes. We examined parosmia in a population-based sample from the Betula study that was conducted in Umeå in northern Sweden (baseline data collected in 1998-2000). We used a sample of 2168 individuals

aged 35-90 years and with no cognitive impairment at baseline. We investigated the prevalence of parosmia and, using regression analyses, its relationship to other olfactory and cognitive variables and quality of life. Benefitting from the longitudinal study design, we also assessed the persistence of parosmia over 5 and 10 years prospectively. Parosmia was prevalent in 5% of the population (n=104) and was often co-occurring with phantosmia ("olfactory hallucinations"), but was not associated with lower self-rated overall quality of life or poor performance on olfactory or cognitive tests. For some individuals, parosmia was retained 5 years (17%) or even 10 years later (10%). Thus, parosmia is relative common in the population, and can be persistent for some individuals. This work provides rare insights into the expected impact of, and recovery from parosmia in the general population, with implications for those who recently acquired parosmia following covid-19. Funding was provided by Knut and Alice Wallenberg Foundation (2016-0229) to J.K.O.

Thu, 16 Sep -08:45 - 10:30

Symposium 8 - Symposium 8

Thu-S8-001

Taste Blindness: How Western Culture Limits Sensory Science

Gabriella Petrick

University of Stavanger, George Mason University

In early September 1912, University of Tokyo chemist Kikunea Ikeda stood before an audience in Washington D.C. and announced his exciting discovery to the International Congress of Applied Chemistry. He told them: "…there is still another quality, which is quite distinct from all these, and must be considered primary [emphasis added], because it cannot be produced by any combination of other [taste] qualities." In an effort to convey to listeners where they might experience this new taste, he suggested: "An attentive taster will find … something common in the complicated taste of asparagus, tomato, cheese, and meat, which is quite peculiar and cannot be classified under any of the above mentioned qualities [sweet, sour, bitter, or briny]. It is usually so faint and overshadowed by other stronger tastes, that it is often difficult to recognize it unless the attention is specially directed towards it." The existence of umami as a basic taste is new to Western scientists yet it has a much longer history in East Asia. Although the other four basic tastes have been

identified in the West since well before the Enlightenment, the number of basic tastes has varied widely across the globe and the centuries. Ancient Zhou philosopher Yen Tzu noted the doctrine of five flavors, which included hot as a basic taste, whereas Qing commentators noted as few as six and as many as nine. Based on the amino acids, umami has a distinctly East Asian pedigree as foods eaten throughout the region combine these amino acids in much larger quantities than in Western diets. In other words, Ikeda's and the Japanese palate was trained to experience umami unlike the palates of Western scientists. I call this inability to taste umami and other yet to be known basic tastes "taste blindness." It also applies to other flavors and textures that do not translate from one culture to another. I argue that taste blindness limits the work of scientists in the chemosenses.

Thu-S8-002

Menstruating bodies at work: Intimate Sense-labour and domestic work in India

Ishita Dey

South Asian University

This paper stems from an ongoing collaborative ethnographic journey with a Delhi-based women workers' union known as Shehri Mahila Kamgar Union since 2015. Sheri Mahila Kamgar Union has a membership of 2000 workers employed in informal sector. Since 2015 I have collaborated with this union to understand the working conditions of domestic workers. This paper draws upon some of the conversations I had with domestic workers in 2018 around smells as part of a commissioned art research project on smells of the city by Kiran Nadar Museum of Art. Here, I choose to focus on one bodily smell that is at the heart of 'intimate sense – labour' - a term I propose to to understand the role of the senses in the everyday work lives of intimate labor. At the heart of domestic work lives is the everyday erasure of smells in the intimate corners and places of a domestic space separated by caste, class, religion, and gender. These acts of erasure of smells are socially coded. This paper draws upon workers' accounts of their work lives during menstruation to unpack how social perception of 'mal odours' are constructed and perpetuated through stigmatization of gendered laboring bodies involved in Intimate sense-labour. Bodily smells are socially coded. Most work based description carry vivid descriptions about sweating bodies. It is also not a coincidence that in early Marx's writings he did mention that history of labour could well be a history of five senses. However, as David Howes scholarship has shown Marx's discussion on senses comes to a pause with the discussion on alienation. Given that intimate sense –labour revolves around removal of smells how do social perceptions around workers' bodily smells shape labouring conditions around intimate sense-labour. By highlighting the social stigma around menstruation in

the work lives of domestic workers I propose to address how ‘mal odours’ are socially and culturally constructed through gendered bodies at work.

Thu-S8-003

Politics, management and a science of subjectivity, or: sensing beer, margarine and water in the peripheral nation of Sweden.

Daniel Normark

Uppsala STS, department of economic history Uppsala university

This presentation summarizes findings from three historical object-biographies on flavor. In these cases, flavor was questioned, investigated and stabilized as an explicit quality of the material itself. Furthermore, the examples show how increased understanding and subsequently control of flavor affected the production and consumption of theses goods. From 1917 to the mid 1960s the examples show an increased use of scientific methods, but rather than confirming an expansion they provide a more nuanced ambivalence of the limits of science. In the aftermath of World War I the flavor of beer became politically contested which led to a state-run investigation of the link between alcohol and the flavor of beer. Flavor became political. When looking at margarine flavor became a quality of control. Initially as a means of controlling produces but expanding into an organizational system of management and financial incentive. Thus, between the 1940s to the 1960 the Swedish margarine company created a division of sensory management. Finally, as a public good, water became a topic of investigation of psychologists (David Katz) and physicians (Yngve Zotterman). Both researchers created their own assemblage of technical objects of “water tasting” while simultaneously addressing the same epistemic thing i.e. “the water taste”. The story reveals the ontological difference between the effort of meretriciously capture the neural response of water, controlling the technologies, stimuli and bodies for used for manipulation or the phenomenological investigation of psychophysical responses taking place in the encounter with water as fully subjective science. Taken together, the cases of sensory science endeavors highlight the importance of subjectivity (vs objectivity) as a teleological goal of science. One could argue in line with the philosopher Edmund Husserl that, in order to understand the world, we are dependent on science of subjectivity as much as science of objectivity.

Thu-S8-004

Catalyzing the decolonization of laboratory research through collaborations with artists

Lauryn Mannigel

Media Arts & Sciences PhD program at Arizona State University

This talk presents part of my interdisciplinary arts-based Ph.D. research in Media Arts and Sciences at Arizona State University and critically explores culturally sensitive and inclusive art-science methods and techniques. The aim of this research is to diversify, democratize, and decolonize perception and knowledge production about the way we think, embody, and express, or communicate, our experiences of others' body scents. The central objective of my talk is to show how inter-/multi-/cross- or transdisciplinary collaborations between scientists and artists can contribute to decolonizing the knowledge production of chemosensory laboratory studies beyond the boundaries of academic disciplines. As a result, these collaborations can expand critical reflection of current methods in chemosensory laboratory studies by further advancing the development of new and ecologically valid methods that embrace the complex diversity of people's real-life context. This talk consists of two parts. First, I will further expand upon how traditional practices present in scientific research can reduce knowledge production in the field of social/chemical communication. Moreover, I will discuss Jasper de Groot, Ilja Croijmans, and Monique Smeet's critique (2020), which focuses on how the smell of other people beyond Western, educated male citizens of industrialized, rich, and democratic countries has been neglected in these traditional studies. Now aware of these above-mentioned restrictions, these scientists are starting to reach out to work with a wider range of cultural and gender diversity (ibid). Secondly, this talk will present a selection of art projects to show how they challenge issues surrounding objectivity and reductionism of scientific research. In this regard, I will explain how these art projects implement Donna Haraway's idea of situated knowledge (1988), and how they can inform the creation of new decolonized tools for scientific research.

Thu, 16 Sep -11:00 - 13:00

Symposium 9 - Symposium 9

Thu-S9-001

The Duality of Olfactory Language

Robert Pellegrino [1, 3], Thomas Hörberg [2], Jonas Olofsson [2], Curtis Luckett [1]

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Olfactory research in humans has largely focused on odors perceived via sniffing, orthonasal olfaction, while ignoring odors perceived from the mouth, retronasal perception. Prior work on retronasally presented odors use animal models and focus mainly on odor sensitivity, but little is known about retronasal olfactory perception and cognition in humans. In this study, we compared orthonasal and retronasal odor presentation routes to investigate differences in odor descriptions. Thirty-six individuals participated in a within-subjects study using twelve odors (varying in pleasantness and edibility) in perceptual and semantic tasks. As expected, we found route-dependent differences in perceptual odor quality (pleasantness, edibility, and familiarity ratings), and a better ability to identify odors during orthonasal presentation. Additionally, more concrete (and source-based) language was used when describing odors presented orthonasally. Exploratory analyses revealed that while orthonasal odors were described with words that had visual associations, retronasal odors were described with words that had tactile associations. Interestingly, sensitivity and intensity did not explain these observed route-dependent differences in descriptor usage, suggesting cognitive and linguistic processes differ between odors presented orthonasally and retronasally. Our results show that olfaction is in fact a dual sense, in which the routes change the perception of an odor.

Thu-S9-002

Foraging minds: multisensory expressions of a high-calorie bias in human spatial memory

Rachelle de Vries, Emely de Vet, Kees de Graaf, Sanne Boesveldt

Wageningen University and Research

Human memory did not evolve in a vacuum. Rather, memory systems were shaped by natural selection to solve fitness-relevant problems, such as the efficient location of valuable calorie-dense foods. We explored whether a high-calorie bias in human spatial memory exists, and can be reliably observed across sensory modalities, participant populations, and experimental paradigms. In two lab studies with distinct samples of 88 participants, individuals had to re-locate foods on a map in a computer-based spatial memory task using visual (Study 1) or olfactory (Study 2) cues that signaled (sweet and savory) high- and low-calorie items. Individuals consistently displayed lower pointing errors (i.e. enhanced memory) for locations of high-calorie versus low-calorie foods (*Study 1*: 121.6 vs 137.8 pixels; $F(1,4049) = 8.25$, $p = .004$; *Study 2*: 118.3 vs 152.7 pixels; $F(1,1240) = 18.43$, $p < .001$) – regardless of hedonic evaluations, familiarity with foods, or encoding time. In a final field-based experiment, we covertly tested the food spatial memory of 512 individuals who navigated a maze-like food setting, and either ate (high- and low-calorie) food products (N=258;

multisensory environment [ME]), or smelled corresponding food odors (N=254; olfactory environment [OE]), at eight spatially dispersed pillars. Individuals incidentally learned and more frequently re-located high-calorie stimuli to correct pillar locations (*ME*: 0.63 vs 0.57 proportion correct relocations, χ^2 (1) = 9.35, p =.002; *OE*: 0.36 vs 0.30, χ^2 (1) = 6.88, p =.009) – while controlling for explicit liking, desirability, and familiarity with foods. The high-calorie spatial memory bias was also equally expressed in both sensory environments – even where solely odor information was available. Taken together, human spatial cognition seems to be optimized for ancestral priorities of energy-efficient foraging. This research was financially supported by the Edema-Steernberg Foundation and the Netherlands Brain Foundation.

Thu-S9-003

Flavor imagery in consumers and experts

Ilja Croijmans

Utrecht University

People rely on descriptions and images when shopping online. This works when buying anything from a phone cover to a sportscar, but may provide insufficient information when seeking specific smells or flavors, for example in scented candles, wine, beer, cheese, or coffee. People, even experts, find it difficult to describe smells and flavors, although experts, through experience, are more consistent and more accurate in their descriptions. At the same time, consumers have difficulty imagining smells and flavors from a description: the chemical senses are often ranked as being least vivid in people's imagination. This suggests an intricate relationship between olfactory cognition, more specifically language and imagery, and expertise. This relationship is explored in a series of (online) studies on mental imagery. First, we established that experts are better at imaging smells and flavors in their domain of expertise. Next, we investigated the relationship between being able to imagine smells, and the ability to describe flavors. The results suggest some interaction between imagery and language. The novice consumer side is explored next: Can imagery ability distinguish consumers and their online purchase behavior based on flavor descriptions? We show consumers can be high and low imagers, but a wine flavor description seems to overrule other information presented – suggesting that also in the mind of the consumer, language and imagery are distinct. Finally, what type of coffee flavor descriptions are most imaginable, and are most successful to sell coffee online? In this last study, we compared different types of coffee descriptors, showing that more concrete language is more imaginable. The context of the words within the flavor description also matter for consumers when buying online. The findings of these series of experiments are discussed in relationship to sensory marketing and embodied cognition.

Thu-S9-004

Smell as knowledge-making: How wine experts deduce place of origin and production methods from wine aromas

Qian Janice Wang

Aarhus University

While the practice of explicitly deriving knowledge from odours is largely overlooked in Western society, it is taught to, and practised by, those in specialised roles such as perfumers and wine experts. In this talk, I will draw on my experience as a wine educator and competitive blind wine taster to illustrate how wine aromas can be interpreted to denote the place of origin and production methods. This deductive tasting method is used, for instance, in Master of Wine and Master Sommelier exams, where candidates are required to identify viticultural and vinification practices of wines tasted blind. By giving an example of how smell epistemology is practised in real life, I aim to inspire future research in odour cognition to go beyond instinctive chemosensory communication.

Thu-S9-005

The cognitive representation of odour in anosmia

Laura Speed [1], Behzad Iravani [2], Johan Lundström [2], Asifa Majid [3]

[1] Radboud University, [2] Karolinska Institutet, [3] University of York

Language and olfaction are thought to be weakly connected: western languages like English have few words to describe olfactory experience and speakers have difficulty naming odors. It has also been suggested that odor and language are weakly connected during language comprehension. Embodied accounts to language suggest word meaning is represented as sensory simulation, but so far there is little evidence of olfactory simulation during language processing. In order to directly test for a role of olfaction in word meaning, we compared performance on a set of pre-registered language tasks in 57 participants with acquired anosmia and 56 matched normosmics. Participants completed a lexical decision task with odor (e.g., lavender), taste (e.g., basil), and vision-related nouns (e.g., brick). We found no difference in response time or accuracy between the two groups. Next, participants completed a semantic similarity judgment task with odor-, taste-, and vision-related words. Participants had to judge which of two words was more similar in meaning to a target word (e.g., is patchouli or vinegar more similar to menthol?). Anosmics were overall slower and more accurate in the task, but this did not differ across word type. However, in an implicit memory

task, anosmics remembered more odor-related nouns than control participants. Anosmics also rated odor- and taste-related nouns as more positively valenced on a seven-point valence scale than normosmics did. Together, these results suggest that olfactory simulation is not critical to the representation of odor-related language, but odor-related language is more salient and emotional to anosmic participants. Since no detriment to olfactory language was found in anosmics, this suggests odor-related language is not grounded in odor perception. Odor and language are weakly connected in language comprehension too.

Thu-S9-006

DeepNose: Using artificial neural networks to represent the space of odorants.

Ngoc Tran, Sergey Shuvaev, Daniel Kepple, Alexei Koulakov

Cold Spring Harbor Laboratory, Cold Spring Harbor, NY

The olfactory system employs an ensemble of odorant receptors (ORs) to sense molecules and to derive olfactory percepts. We hypothesized that ORs may be considered 3D spatial filters that extract molecular features relevant to the olfactory system, similar to the spatial filters employed in other modalities. If so, the composition of OR ensemble can be understood by training such filters using conventional artificial intelligence methods and large-scale databases of 3D molecular structures. We trained artificial neural networks to represent the chemical space of odorants and used this representation to predict human olfactory percepts. First, we trained an autoencoder called DeepNose to deduce a compressed representation of odorant molecules based on their 3D spatial structure. Next, we tested the ability of DeepNose features in predicting human odorant percepts based on 3D molecular structures alone. Finally, we finetuned the DeepNose network to better represent perceptual properties of odorants defined as semantic descriptors. We found that, despite the lack of human expertise, DeepNose features led to perceptual predictions of comparable or higher accuracy to molecular descriptors often used in computational chemistry. We propose that DeepNose network can use 3D molecular structures to yield high-quality predictions of human olfactory percepts and can help understand the factors influencing the composition of ORs ensemble.

Thu, 16 Sep -11:00 - 13:00

Symposium 10 - Symposium 10

Thu-S10-001

What is a connectome, and what can it be good for

Wen Li

Florida State University

The brain is a highly complex system that is organized by large-scale connectomes. In the sensory brain, specific connectomes, i.e., intrinsic neural networks (ICNs), have been well-established for vision, audition, and somatosensation. However, the definition of the chemosensory connectome has lagged. Leveraging the large and high-quality resting-state functional magnetic resonance imaging (rs-fMRI) dataset of nearly 900 participants from the Human Connectome Project (HCP), we combined resting-stating functional connectivity analysis with graph-theoretical analysis to identify the human olfactory connectome/network (Arnold et al., 2020). Our study demonstrated that (1) the olfactory neural network consists of cortical and subcortical regions widely distributed in the frontal and temporal lobes; (2) the olfactory network is organized by three subdivisions—the sensory, limbic, and frontal subnetworks; and (3) the olfactory network resembles a highly efficient system characterized by a high degree of global integration balanced with a high degree of local segregation (i.e., circuit specialization). Highlighting its reliability and generalizability, the composition of the olfactory network mapped closely onto one that was extracted from our independent rs-fMRI dataset. Moreover, the degree of local segregation positively predicted olfactory discrimination performance in our sample. The composition and topological organization of the human olfactory network would illuminate the machinery underlying olfaction, the most intriguing sense for its heterogeneous and yet harmonized functions in sensory perception, emotion, neuroendocrine, and homeostasis. Therefore, we applied this olfactory network composition and topological principles to fMRI responses to odor and sweat stimuli of aversive and neutral emotion. Findings from this new study provide important connectome-level insights into the functional architecture underlying this uniquely multipurpose system of olfaction.

Thu-S10-002

The odor identity can be decoded from the connection between olfactory bulb and piriform cortex in humans

Behzad Iravani, Artin Arshamian, Johan Lundström

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Brain networks, including olfactory system, communicate internally and externally via neural oscillations. Specifically, two key nodes of olfactory system–the olfactory bulb and the piriform

cortex –have been demonstrated in non-humans to communicate with each other via neural oscillations to form olfactory percept. Nevertheless, the communication of these two critical olfactory nodes is not well understood in humans. We used our recent developed and validated EEG-based method to assess the OB-PC communication in healthy human participants. With the help of source reconstruction method, the cross-spectrogram of the OB and PC source signals was evaluated, where we found that there is evaluation in the frequency of the OB-PC connection from early gamma to late theta/delta bands. Moreover, we further found that there is a bottom-up information flow from the OB to the PC in the beta and gamma frequency bands, while top-down information from the PC to the OB is facilitated by delta and theta oscillations. Critically, using machine learning methods, we demonstrate that there was enough information to decode odor identity above chance as early as 100ms after odor onset from the level of OB-PC connection in low gamma band. These data illuminate further the critical role of bidirectional information flow in human sensory systems to produce perception. Nevertheless, it cannot be yet fully determined what specific odor information is extracted and communicated in the information exchange and future studies are needed to address this matter adequately.

Thu-S10-003

A mesoscopic connectome for taste processing in non-human primates revealed by event-related functional magnetic resonance imaging

Renee Hartig [1, 2, 3], **Ali Karimi** [4], **Henry Evrard** [1, 2, 5, 6]

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The examination of central taste processing affords the unique opportunity to study the interactions between sensory regions, central integrators, and effector targets. Here, the mesoscopic taste processing connectivity was revealed by single voxel- and region-level univariate regression modeling of the underlying BOLD signal during the delivery of sweet, sour and salt tastants. We investigated the functional information processing across anatomically defined cortical and subcortical regions using ultra-high field (7T) functional magnetic resonance imaging in anesthetized macaque monkeys. A regional beta-series correlation method was implemented to assess functional connectivity across brain regions involved in taste processing, collectively forming

the taste connectome. Our analysis showed consistent connectome-wide correlations across all three tastants and significant callosal connections between regions across hemispheres. A seed-based functional connectivity analysis was additionally conducted to examine the role of three different insular cortex sub-regions (mid-dorsal, anterior dorsal, and anterior ventral insular cortex) in taste processing. Comparing the connectivity profiles of these insular sub-regions, the anterior ventral insular cortex activity was most correlated across the taste connectome nodes, extending from the insular cortex to the dorsal striatum, amygdala and prefrontal cortex. An unbiased modularity analysis was also performed on the graph of the taste connectome using community detection methods. These results revealed a hierarchical arrangement of the connectome's subcortical and cortical nodes, with three regional modules connected across the entire taste connectome. In whole, our results indicate a consistent interaction network for sweet, sour and salt taste qualities as well as a bilaterally inter-connected scheme for modular taste processing across the brain.

Thu-S10-004

How to study the chemosensory connectome - is there a consensus on best practices?

Maria Geraldine Veldhuizen [1], Cinzia Cecchetto [2], Florian Ph.S Fischmeister [3, 4]

[1] Mersin University, Turkey, [2] University of Padova, Italy, [3] Graz University, Austria, [4] Medical University of Vienna, Austria

The use of connectivity methods has increased exponentially in neuroimaging, and this trend is also visible in chemosensory neuroimaging. Here we scope general trends in chemosensory connectomics, we outline recent best practices from the general field of connectomics and make recommendations most pertinent to challenges posed in chemosensory connectomic studies.

Thu-S10-005

Odors mediate the visual categorization of ambiguous stimuli in the human brain

Arnaud Leleu [1], Diane Rekow [1], Karine Durand [1], Jean-Yves Baudouin [2]

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des Vulnérabilités (PsyDÉV), Institut de psychologie, Université de Lyon (Lumière Lyon 2), 5, avenue Pierre-Mendès-Fr

Visual categorization is the brain ability to rapidly and automatically assign a visual stimulus to a given category despite more or less ambiguous inputs. Whether visual categorization can be mediated by non-visual inputs, such as odors, to resolve ambiguity, remains poorly understood. Here we test the influence of odor contexts on category-selective neural responses, expecting that congruent odors facilitate the categorization of ambiguous visual inputs. Scalp electroencephalogram (EEG) was recorded in 26 participants while natural images of various objects were presented at 12 Hz (i.e., 12 images / second). Variable exemplars of a target category were interspersed every 9 stimuli to tag category-selective EEG responses at 12/9 = 1.33 Hz. The target category was either unambiguous (2 categories: human faces and cars) or ambiguous (facelike objects perceived either as nonface objects or faces). Odor contexts (body, gasoline or baseline odors) were diffused implicitly during visual stimulation. We identify clear category-selective responses to every category over the occipito-temporal cortex, with the largest response for human faces and the lowest for facelike objects. Importantly, body odors enhance the neural response to the ambiguous facelike objects, especially for participants reporting the perception of an illusory face in these stimuli. In contrast, odors do not modulate other category-selective responses, nor the general visual response recorded at 12 Hz, revealing a selective facilitating influence on the visual categorization of congruent ambiguous stimuli. Overall, these observations demonstrate that the human brain actively uses cues from the other senses to readily categorize ambiguous visual inputs, and that olfaction, which has long been held as poorly functional in humans, is ideally suited to disambiguate visual information.

Thu-S10-006

Systematic findings on the functional connectome of chemosensory perception.

Robert Pellegrino [1], Michael Farruggia [2, 3], Dustin Scheinost [2, 4, 5, 6]

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Connectivity approaches are needed to understand chemosensory neuronal processes via functional mechanisms and interactions between related brain regions. Chemosensory perception arises from three distinct senses that interact with external chemical information, smell, taste and

chemesthesis. Several systematic reviews exist for each modality, even multisensory percepts like flavor, showing related brain regions; however, reviews to date have only focused on spotlight analysis rather than functional connectivity. Here, we provide a systematic review of chemosensory studies using connectivity techniques of regional or brain-wired connectivity to define functional networks in the brain. We use a proof of concept analysis, Connectome-based Predictive Modeling (CPM), to show how connectivity considering a large-scale network can reveal novel insights regarding taste processing in particular. Lastly, we discuss the need for researchers to openly publish data and methods to increase accuracy and generalization of models developed using functional connectivity.

Thu, 16 Sep -14:30 - 16:15

Symposium 11 - Symposium 11

Thu-S11-001

Olfaction in larval *Anopheles gambiae*

Olena Riabinina

Durham University, UK

Malaria is a vector-borne disease that currently affects half of the world population and leads to >400,000 deaths/year. Larval and adult mosquitoes use olfaction to locate their human hosts, food sources, aquatic habitats and to avoid harmful substances in their environment. Due to the lack of suitable research tools until very recently, little is known about how individual smell-detecting neurons of mosquitoes respond to odorants. Here I will present the new methods to study how the larvae of malaria mosquito A.gambiae use their sense of smell to detect insect repellents. I will answer this question by monitoring behaviour of wild-type and olfactory impaired larvae, and by recording activity of their smell-detecting neurons with the help of a fluorescent indicator. Findings of this project will inform future work on modifying mosquito preference to smells by genetically changing how their neurons function, as a potential method to control malaria.

Thu-S11-002

Mating increases Drosophila melanogaster females' choosiness by reducing olfactory sensitivity to a male pheromone

Jean-Christophe Billeter

University of Groningen Netherlands

Females that are highly selective when choosing a mate run the risk of remaining unmated or delaying commencing reproduction. Low female choosiness would therefore be beneficial when males are rare, but it would be maladaptive if males become more frequent; how can females resolve this issue? Polyandry would allow mating status-dependent choosiness, with virgin females selecting their first mate with little selectivity and becoming choosier thereafter. This plasticity in choosiness would ensure timely acquisition of sperm and enable females to increase offspring quality during later mating. Here, we show that Drosophila melanogaster females display such mating status-dependent choosiness by becoming more selective once mated, and identify the underlying neurohormonal mechanism. Mating releases juvenile hormone, which desensitizes OR47b olfactory neurons to a pheromone produced by males, resulting in increased preference for pheromone-rich males. Besides providing a mechanism to a long-standing evolutionary prediction, these data suggest that intersexual selection in D. melanogaster, and possibly in all polyandrous, sperm-storing species, is mainly the domain of mated females as virgin females are less selective. Juvenile hormone influences behaviour by changing cue responsiveness across insects, the neurohormonal modulation of olfactory neurons uncovered in D. melanogaster provides an explicit mechanism for how this hormone modulates behavioural plasticity.

Thu-S11-003

The role of olfaction in female aggression.

Miguel Gaspar, Sophie Dias, Maria Luisa Vasconcelos

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Aggression is a fundamental, innate part of animal behavior, prevalent throughout the animal kingdom. The outcome of successful aggressive encounters can endow individuals with increased social status, as well as access to territory, resources, and potential mates. Roughly, aggression in *Drosophila* males is modulated by the olfactory receptors Or67d and Or65a, which regulate the acute and chronic levels of aggressive arousal. Female *Drosophila* aggression, on the other hand, is not well understood. In this study, we introduce a novel context that reliably induces female aggression: by placing two females with a male we have been able to consistently observe

aggression between the uncopulated female and the copulating pair. Using this simple assay we show that female aggression also requires olfaction. The aggressive display is at least partially dependent on activity of Or47b neurons, which detects fly-produced odorants. Interestingly, activity of Or67 neurons does not play a role in female aggression in this context. Additionally, the presence of food odor stimulates females to be more aggressive. Finally, we show that both mated and uncourted females display significantly less aggression, demonstrating that both external stimuli and internal states modulate female aggressive behavior. This work was supported by Fundação para a Ciência e a Tecnologia (FCT, PD/BD/105943/2014)

Thu-S11-004

Intra-specific individuality and modulation of olfactory circuits in *Drosophila*

Florencia Campetella, Karen Rihani, Bill S. Hansson, Silke Sachse

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Most species rely heavily on olfaction to ensure their survival and reproduction. In addition, the animal's previous experience has a strong impact on how odors are processed and perceived in order to adapt to a changing environment. While we start to understand how odors are coded and processed by the underlying neuronal circuitry, the impact of modulation and the role of intra-specific variation still remains largely elusive. We are therefore studying how the olfactory circuitry is modulated by previous experience and associative learning as well as analyzing intra-specific variability at the circuit level between different individuals in the fly brain. The vinegar fly *Drosophila melanogaster* represents a premier model system for studying olfactory processing since it exhibits a stereotyped architecture which is similar to its mammalian counterpart, but is less complex and highly tractable as well as susceptible to genetic manipulations. By exploiting these genetic techniques and linking them to neurophysiological and behavioral methods, we are able to demonstrate that certain olfactory circuits are strongly affected by associative learning and can even be oppositely modulated by aversive and appetitive conditioning. The talk will summarize our recent insights into the modulation and processing strategies of the olfactory circuitry of *Drosophila*.

Thu-S11-005

Olfactory ecology of the migratory locust, *Locusta migratoria*

Bill S Hansson [1], **Hetan Chang** [1], **Xingcong Jiang** [1], **Anjana Unni** [1], **Eleutherios Dimitriou** [1], **Juergen Rybak** [1], **Kang Le** [2], **Silke Sachse** [1], **Markus Knaden** [1]

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The migratory locust is one of the most devastating insects of the world, with swarms emptying huge areas of crops and pasture. The locust also has a very different olfactory architecture as compared to other insects, with more than a thousand micro glomeruli in the antennal lobe, branched axons of olfactory sensory neurons and unorthodox morphology among both projection and local interneurons. In a concerted effort, using state-of-the-art methodology, we set out to investigate the system from beginning to end; from olfactory receptors to behavior. By introducing locust olfactory receptors into the *Drosophila* empty neuron system we could gain insight into the specificity of single receptors. To have a relevant stimulus spectrum we identified molecules emanating from all life stages of the locust and of preferred and not-preferred food souces. In this way we could deorphanize most of the ca. 100 receptors. Among the receptors we discovered one that responded specifically to the pheromone phenylacetonitrile (PAN). In behavioral experiments we revealed the effect of this compound. By using CRISPR-cas9 tecnhnique we could then knock out the PAN receptor and show that the behavioral traits were abolished. In ongoing experiments we are now using genome editing to introduce calcium dynamics indicators in olfactory receptor neurons, allowing us to observe antennal lobe processing of relevant odor information. This project is a collaborative venture between Max Planck and the Chinese Academy of Science.

Thu, 16 Sep -14:30 - 16:15

Symposium 12 - Symposium 12

Thu-S12-001

Adult olfactory neurogenesis: of mice and men

Bradley Goldstein

Duke University School of Medicine

The olfactory epithelium in the nose houses the olfactory sensory neurons, serving as the peripheral organ for smell. Acquired injury or loss of olfactory neurons can occur due to trauma, infection or inflammatory insults. Fortunately, a remarkable repair capacity exists, in the form of basal stem cells capable of reconstituting the epithelium following damage. This system has been well-studied in rodent models, providing insights into the mechanisms maintaining normal neuronal turnover or wholesale neuroepithelial repair following experimentally-induced injury. However, acquired olfactory disorders occur in humans, suggesting that reparative mechanisms are imperfect. In an effort to better understand acquired olfactory disorders and consider possible treatment strategies, we have utilized new approaches to analyze human olfactory epithelium. For this symposium on regenerative activity in the gustatory and olfactory systems, we will summarize findings investigating neurogenesis in rodent and adult human olfactory epithelium, with a focus on efforts to begin to translate advances to address human sensorineural olfactory disorders.

Thu-S12-002

How to Fix a Broken Nose

James Schwob

Tufts University School of Medicine

Many forms of olfactory dysfunction, particularly the all-too-frequent age-related decline in ability and the loss that can occur after URI, are associated with pathological alterations of the normal composition of the olfactory epithelium. Two forms of epithelial abnormality are neurogenic exhaustion, in which the active stem and progenitor cell population of globose basal cells (GBCs) as well as their progeny, the olfactory sensory neurons (OSNs), become depleted, and respiratory metaplasia, in which what was olfactory epithelium adopts the cellular composition and appearance of respiratory epithelium. In both cases, the population of reserve stem cells, the horizontal basal cells (HBCs), persist but remain unhelpfully dormant. A potential strategy for repairing the periphery activates the HBCs and directs their progeny toward transdifferentiating into GBCs which then repopulate the OSNs. Key to the activation process is the master transcription factor DNp63, and it is necessary and sufficient to eliminate or diminish its amounts for activation of the HBCs to proceed. Efforts toward that end entail manipulations of Notch signaling and directed proteolysis of p63, both of which are known to participate normally in the regulation of its expression and concentration.

Thu-S12-003

Neuronal regulation of adult taste stem cells

Peihua Jiang

Monell Chemical Senses Center

Maintenance of taste tissues requires continuous replacement of senescent taste cells with new ones generated from adult taste stem cells. This process depends on taste bud innervation, first noted more than a century ago. Until recently, the molecular mechanism underlying this process remained unclear. Prompted by our observation that single Lgr5+ taste stem/progenitor cells can give rise to all different types of mature taste cells in an ex vivo culture system ("taste organoids") in the absence of nerve input, which suggests that one (or several) of the components in the defined culture medium may be the principal gustatory neuron-produced factor, we set out to identify such factor. We focused on R-spondin, the ligand for the Lgr5 receptor. Our in situ hybridization study showed that R-spondin 2 is expressed in gustatory neurons. Using a gustatory nerve transection model and adenovirus-encoded R-spondin, we showed that exogenous R-spondin can promote taste cell generation despite denervation. Using the organoid culture system, we further showed that R-spondin is required for taste cell generation. R-spondin interacts not only with Lgr5 or its analogs Lgr4/6 but also with two E3 ligases Znrf3/Rnf43 to regulate Wnt signaling (Lgr4/5/6 – positive regulators, Znrf3/Rnf43 - negative regulators). Therefore, we hypothesized that Znrf3/Rnf43 may serve as a brake, controlled by gustatory neuron-produced R-spondin, for maintaining taste tissue homeostasis. Consistent with this model, taste cell hyperplasia occurred in mice lacking Znrf3/Rnf43 in taste stem/progenitor cells, mirroring the effect of exogenous R-Spondin. We further demonstrated that ablating Znrf3/Rnf43 renders neuronal regulation of taste tissue homeostasis dispensable: regeneration of taste cells occurred in the double knockout mice even in the denervation model. In summary, the ternary interaction of R-spondin, Lgr4/5/6, and Znrf3/Rnf43 plays a key role in neuronal regulation of taste stem cells.

Thu-S12-004

Single-cell RNA-sequencing analysis of mouse circumvallate papilla reveals a role for Notch signaling in taste cell fate decisions

Dany Gaillard [1], Eric Larson [2], Lauren Shechtman [1], Trevor Isner [1, 3], Jennifer Scott [1], Theresa Keeley [4], Austin Gillen [5], Peter Dempsey [6], Linda Samuelson [4], Linda Barlow [1, 3]

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Taste buds are composed of functionally heterogeneous taste bud cells (TBCs) that transduce sweet, sour, salt, umami, and bitter stimuli. In addition, each bud houses a large proportion of glial-like support cells, i.e., Type I TBCs. All TBCs continually renew from adult lingual stem cells that also produce the non-taste epithelium of tongue; however, the lineage relationships of these cell types, as well as factors that regulate acquisition of these many distinct cell fates are largely unexplored. We have used analysis of single cell transcriptome data of adult mouse circumvallate taste papilla to identify stem populations and the subsequent lineage steps that lead to production of taste and non-taste epithelial cell types. Now, we employ CellChat (http://www.cellchat.org/) to bioinformatically identify active signaling pathways and the polarity of signaling for specific lineage steps, i.e., ligand-expressing signaling cells and receptor-expressing cell populations. This analysis confirms and expands our understanding of WNT and Hedgehog signaling in taste homeostasis, and identifies a host of new candidate regulatory pathways that likely control different aspects of taste bud cell renewal. In particular, CellChat analysis suggests that Notch signaling functions iteratively in taste epithelium to (1) regulate lingual stem cells and (2) drive differentiation of Type I TBCs. We are testing these hypotheses of Notch function in vivo using molecular genetic mouse models to activate Notch signaling at distinct lineage steps, and in vitro, treating lingual organoids derived from adult taste stem cells with small molecule Notch pathway inhibitors and activators.

Thu-S12-005

Insulin, its receptor and regeneration of the olfactory epithelium

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Olfactory sensory neurons (OSNs) can regenerate after injury of the olfactory epithelium (OE). Insulin is a neural growth factor that plays important roles in neuronal survival and maturation. Insulin receptors are expressed both in the OE and olfactory bulb, but it is remains poorly understood how insulin signaling affects the regeneration of OSNs. We examined how insulin deficiency impedes the functional recovery of the OE after injury in adult mice using a type 1 diabetic

mouse model. To induce type 1 diabetes, streptozotocin (STZ) was administered to selectively ablate pancreatic β cells, resulting in hypoinsulinemia. To injure the OE, methimazole, which induces apoptosis of OSNs was injected intraperitoneally. At day 7 after injury, no significant structural changes of the OE were observed between STZ- and control (saline-administered) mice. However, at day 14 and 28 after injury, remarkably fewer regenerated mature and more apoptotic OSNs were found in STZ-mice. STZ-mice showed smaller odorant-induced electroolfactogram (EOG) responses, a smaller number of c-Fos-positive cells in the olfactory bulb following odorant stimulation, and impaired performance in an odor-guided task at day 28 post-injury. Intranasal insulin administration during days 8 – 13 (unlike during days 0 – 6) after injury rescued the recovery of the OE in STZ-mice to levels similar in control mice. During day 8 – 13 after injury, insulin receptor expression was upregulated and the intranasal application of an insulin receptor antagonist slowed OE regeneration even in control mice. Furthermore, OE regeneration in control mice was enhanced by nasal insulin application during this period. These results suggest that newly generated OSNs have a high dependency on insulin signaling required for their maturation during the critical time window on days 8 – 13 after injury. Therefore, insulin signaling is a key factor for OE regeneration following injury.

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